AN ESSAY

ON THE

BLOOD IN DISEASE.

BY

G. ANDRAL.

TRANSLATED FROM THE FRENCH

BY

J. F. MEIGS, M.D., AND ALFRED STILLÉ, M.D.


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PATHOLOGICAL HÆMATOLOGY.

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BY G. ANDRAL,

PROFESSOR OF GENERAL PATHOLOGY AND THERAPEUTICS IN THE UNIVERSITY OF PARIS, ETC. ETC.

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Non ideo analyses sanguinis utilitate suâ destituuntur, dùm sapienter noverimus spes nostras recidere, neque plura docere quàm a naturâ discimus.—HALLER, *Elem. Physiol.* lib. v.

PHILADELPHIA:

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ESSAY

UPON

PATHOLOGICAL HÆMATOLOGY.

Hæmatology is that branch of the natural sciences the subject of which is the study of the blood. This expression is not a new one in science: about a century since, an author now but little known, Thomas Schwenke, published, under the title of Hæmatology, a treatise as complete as it could then be, upon the blood considered in its state of health and of disease.*

Before this author, and since his period, many works, some theoretical, some experimental, have been published on the blood; their simple enumeration would be a considerable undertaking, and one not without utility; such however is not the end that I seek: but I come to add to all these works, of various importance, a new one, in which I design to make known the alterations that the blood has presented me in different diseases, under the triple view of its physical properties, and of its chemical and microscopic constitution. I shall endeavour to estimate the importance of these alterations in regard to semeiology and pathogeny; and I shall discuss finally the value of the methods that have been followed at different periods for the purpose of discovering the facts of pathological hæmatology.

* Thomæ Schwenk Hæmatologia, sive sanguinis historia, experimentis passim superstructa, in 8° Hagæcomitum, 1748.

Already in two memoirs read at the Academy of Sciences in 1840 and 1842, I have exhibited the results that I obtained, in seeking to appreciate the variations of proportion, that some of the principles of the blood, to wit, the fibrine, the globules, the solid elements of the serum, and the water, may offer, whether in disease, or in different states of the physiological condition. To accomplish these researches I have followed the method indicated by M. Dumas, one which he himself advised me to have recourse to, as answering the end that I sought to attain. May he permit me to express to him on this occasion my gratitude for all his kind advice.

In the work that I now publish, I have sought to give a greater development to the facts and ideas contained in my preceding memoirs: there will be found in addition a certain number of results that I have obtained more recently, and which have not yet been made public. For many of the details and ciphers I will refer the reader to the two other memoirs;* for I do not pretend to give to the world a finished and complete essay—even while continuing my researches, I desired to indicate the point to which they had attained, what results they had yielded, and what it may be possible to arrive at, if the pursuit does not become wearisome.

* Recherches sur les modifications de proportion de quelques principes de sang (fibrine, globules, matériaux solides du sérum, et eau) dans les maladies, par MM. Andral et Gavarret (*Annales de chimie et de physique*, tome LXXV). Recherches sur la composition du sang de quelques animaux domestiques dans l'état de santé et de maladie, par MM. Andral, Gavarret et de la Fond (*Annales de chimie et de physique*, 3d serie tom. v.).

The results detailed in these two memoirs, as well as those contained in this new work, are the fruit of researches common to myself and to M. Gavarret, to whose learned and devoted collaboration I am greatly indebted. For the facts relating to animals, M. de la Fond, professor at the veterinary school of Alfort, kindly lent us the aid of his time and experience.

The method that we have followed, and the results that it has given us, having been the subject of several criticisms, we have thought proper to answer these in a separate work, to which I shall also refer from time to time, and which has for title: *Réponse aux principales objections dirigées contre les procédés suivis dans les analyses du sang, et contre l'exactitude de leurs résultats*, brochure in 8°, 1842, chez Fortin et Masson.

CHAPTER I.

OF THE BEST METHOD TO PURSUE IN THE STUDY OF PATHOLOGICAL HÆMATOLOGY.

It was one of the dogmas professed by the school of Cos, that in order to explain the phenomena of health and of disease, we must take equally into consideration the solids which enter into the composition of the human body, the fluids with which it is so abundantly provided, and the forces which control it. But few physicians however remained faithful to these principles, which Hippocrates has declared in several of his works, and particularly in his book on *ancient medicine;* and we find Galen reproaching his contemporaries with some bitterness, for having broken this beautiful ensemble of the ancient Grecian school, in order to interpose in their explanation of disease, some only the solids, others only the fluids, and others again only the forces which pervade and animate organized matter.* And thus were determined from those ancient times, the three great points of view, which, now abandoned, and now again adopted, have produced the three systems of solidism, humorism, and vitalism.

One of the characteristics, and I venture to say one of the glories of the present medical epoch, is to have understood to

* Hippocrates, cum trifariam hominis elementa divisisset, in continentia, contenta, et ea quæ impetum faciunt. . . ., haud scio quomodo successores ejus unam illam revera divinam Æsculapii medicinam in tres partes sibi cohærentes distribuerint atque divulserint. Alii enim humidis, tum causam eorum quæ secundum naturam habent constitutionem, tum causam eorum quæ præter naturam, solis attribuere, ut Praxagoras et Herophilus. Alii, solidis corporibus initia et elementa attribuentes, ex his tum quæ natura consistunt, tum morborum causas inde capiunt, et Erasistrates et Asclepiades, Athenæi vero et Archigenis imitatores, spiritu solo ea penetrante, tum naturalia consistere ac gubernari, tum morbos universos hoc prius offenso creari dixerunt. (Medicus.)

what incomplete and necessarily erroneous results these minute subdivisions of the science conduce; and, at the same time that it has given a due degree of importance to dynamism and solidism in pathogenic theories, it has returned to the study of the alterations of the blood; it has recognized their existence, and has accorded them an influence in the production of disease. But, singular fact! these alterations, of which the reality and importance are no longer denied by any, are nevertheless scarcely known, and but few facts could be cited in proof of the convictions arrived at on this subject; direct observation of the blood has thus far been much more rarely invoked than theory, and when recourse has been had to observation, it has been made use of most frequently only to study in the sanguine fluid, the simple alterations of its physical properties. But thus we remain ever in the infancy of the science; to progress, we must analyze the blood: such is the idea which guided M. Magendie when, by modifying artificially its composition, he proved that we can by these means create disease. Pathological hæmatology will begin to be enriched with facts of some value, only when the blood of a great number of patients shall have been submitted both to chemical investigation, and that by the microscope. Doubtless, while studying by this double means of analysis the different elements of that fluid, and while thus following them one by one in all their possible variations of proportion and nature, we must not neglect the study of the changes it may undergo in its physical properties; but we soon discover that this latter mode of examination is almost always insufficient, and that when employed alone, without the control of analysis, it may often become a source of error. For we should be unable to give an exact account of the different modifications that the blood is susceptible of in its physical properties, unless we have learned to connect these changes with others more intimate occurring in the composition of that fluid, and of which the first are but the effects. Thus it may happen that the blood shall present an identical appearance, and be equally buffed in diseases as different as are chlorosis on the one hand,

and pneumonia or acute articular rheumatism on the other. But is the blood alike in chlorosis and pneumonia? Does the buff in these two diseases have the same signification? This the simple consideration of the aspect of the fluid could not inform us; analysis alone can reveal it to us, as I shall show farther on. At other times it is the microscope which becomes our chief means of analysis; it is this, for example, which will reveal to us alterations of quality in the globules, or which will show us pus in the blood, etc. Finally, in these difficult researches, where no source of light should be neglected, chemical and microscopic investigation will find at times a useful aid in physiological experiments. By these last, in fact, we can modify in animals the composition of the blood, and as a consequence its physical properties, in such a way as to render this fluid more or less similar to what it is in certain diseases. Once these modifications produced, we observe what are the phenomena that result in different parts of the organism, and we can draw conclusions relative to the influence that modifications of the same nature occurring spontaneously in the blood of man, may exercise in the production of various morbid conditions. It is by acting in this way that M. Magendie has shown the influence that blood, less than usually charged with fibrine, may have in the production of sanguine congestions and hemorrhages. By the direct analysis of the blood of the sick, I have arrived, in this respect, at results similar to his own.

Such are the modes in which we must necessarily proceed, if we seek to give some impetus to pathological hæmatology. Of what use is it, indeed, to waste our time, as has often been done, in mere speculations, on the part played by the blood in the economy, on the reciprocal influence of this fluid upon the solids, or of the solids upon it? Of what use is it again to deduce, by reasoning, the existence of alterations of its composition and their influence in disease, from a consideration of the causes and symptoms of these last? Without doubt we may there find strong arguments to bring forward; but they can conduct only to simple probabilities, or else we should in

this way always remain with notions so incomplete as to be most frequently useless, and sometimes even dangerous. It is by this method that some have supposed the blood to be changed, and this change to be the point of departure of the disease, when this disease recognizes as cause the absorption of a miasm, of a virus, or of a poison. Yet that is only a presumption, and we might just as well admit that the blood, in cases of this kind, serves merely as a vehicle to the deleterious agent which has traversed without altering it, in order to pass on with greater or less rapidity to attack the solids alone. I might cite many other examples of the deplorable uncertainty in which we are forced to remain, while from the nature of the causes or of the symptoms we seek to adduce directly the nature of the alteration that the blood may have undergone; would it have been possible, for example, by this method, to recognize the difference between the alteration of the blood in scurvy and in chlorosis? What has been said indeed of the state of the blood in these two diseases? Nothing more than that it was deteriorated, and on this deterioration all the symptoms of scurvy and of chlorosis were made to depend. But why then are these symptoms so very different? It is because the nature of the deterioration is not the same in the two diseases; in each of them there is a different element of the blood in fault, and thus analysis teaches us that scurvy and chlorosis are not diseases of the same nature, and by this means we can explain the great difference in their symptoms, notwithstanding the fact that a deteriorated blood exists in both. Thus, when anatomy fails to disclose to us any change, chemistry brings it to light, and I doubt not that it will become more and more one of the bases of pathogeny, not only as is the case particularly at present by analyzing the fluids modified by disease, but also by tracing in the solids themselves the important study of the changes in proportion and nature of the elementary principles which compose these solids.

Besides, it is not only in our day that the idea has arisen of seeking the origin of diseases in some alteration of the elementary principles which enter into the composition of the bodies of

animals: this idea was brought to light in the earliest periods of science; but for a long time remained without results, because in place of seeking to establish experimentally the alteration of these principles, nothing more was done generally than to suppose it. The ancient humorism, during every epoch when it has prevailed, was but the exaggerated and hypothetical expression of this idea. It is found entire in the dogmas of the Grecian philosophy, which attributed diseases to a certain number of modifications occurring in the elements, of which it supposed the human body to be primarily composed. This doctrine ruled in science without control from the time of Thales down to that of Galen, and from Galen to the chemists of the sixteenth century. These latter, in destroying the ancient doctrine of the four elements, overthrew likewise the medical theories that were attached to it; but they preserved its original idea; for they also determined that the origin of diseases ought to be referred to a vicious combination, or to some alteration of the simple principles which they thought to have discovered in nature at large, and in organized bodies in particular. They troubled themselves but little, however, to make experiments for the purpose of proving their assertions; what they saw take place in their crucibles, they boldly concluded must occur also in the living body; they made the acids, alkalies and salts, which they had discovered in the organs, react in their interior, without endeavouring by experiment to prove the reality of these reactions; and in this way they arrived in their pathogenic doctrines, at the strangest conceptions: there remains to us for example, a nosology of this epoch, by Schenneman, a disciple of Paracelsus, in which that author makes ten classes of diseases, which he founds upon a certain number of modifications occurring in three principal constituents of the body, to wit: mercury, sulphur, and salt.*

At this period, Sylvius Deleboë sought to found a complete medical system, by ascribing diseases to an alteration of the

* See Sennerti opera, tom. i, de chemicorum cum Aristotelicis et Galenicis consensu ac dissensu liber, cap. iii.

principles which chemistry had just discovered. He assigned a prominent part in the production of diseases to the state of acidity or alkalinity of the humours. One of the most frequent causes of fever, according to him, was an *âcre*, possessed of different chemical properties, which irritated the heart.* He made inflammation to depend upon stagnation of the blood in the vessels, in consequence of which its more volatile and subtile parts which commonly dilute the acid or alkaline portions, evaporated; then these latter became more acrid, produced a hot effervescence, because of the oleaginous molecules they contained, and the blood might in this way arrive at such a degree of inflammation as to be transformed into pus.† These doctrines and this language are scarcely intelligible to us; and yet, amid so many vain hypotheses, one is often surprised to find from time to time propositions which deserve a serious examination, and to which pathological physiology has of late returned. It is in this way that Sylvius explains a considerable number of disorders of the digestive functions, sometimes by the unusual chemical reactions which take place in the stomach or in the intestines, sometimes by the formation in these parts, of an excess of acid, sometimes, on the contrary, by the diminution of the acid or alkaline materials which ought naturally to be formed in the digestive tract.‡ Elsewhere,

* Quolibet acre, nunc acidum, nunc lixivo-salsum, nunc muriatico-salsum, par venas unà cum sanguine ad cor propulsum, atque internè cordis parenchyma mordicans. Francisci Sylvii Deleboe praxeos medicæ liber primus, caput xxvii. de Febribus in genere.

† Arbitror autem incendi ac inflammationem parere sanguinem, quatenus ex ipso in vasis suis valdè distentis, partibusve quibusdam aliis subsistente, hoc est stagnante, mox incipiunt evanescere partes spirituosæ, magisque volatiles ac subtiles tum acidas, tum salinas temperare solitæ; unde utræque acriores factæ acrius in se mutuo insurgunt, effervescentiamque ob partes sanguinis oleosas præsentes calidam excitant; quin paulatim sanguinem ita corrumpunt, ut in pus vertatur. Sylvius Deleboe, loc. cit., lib. i. cap. xl.

‡ Idem, ibid, cap. i, de siti læsa.—cap. vii, de alimentorum fermentatione in ventriculo læsa.—Cap. ix, de nausea, eructatione et vomitu.—Cap. x, de chyli a fœcibus alvinis secretione læsa.—Cap. xi, de vitiosa bilis, et succi pancreatici una cum pituita continuo excitata in tenui intestino effervescentia.—Cap. xiv, de variis intestinorum doloribus.

Might not several of the subjects announced in these titles of chapters be-

Sylvius seeks to account for the fluidity of the blood in malignant fevers and in the plague, by the presence in the mass of that fluid, of an excess of alkaline principles, formed in the economy, or introduced from the exterior; and what occurs rarely in his works, he cites here seven experiments; he says on the one hand, that the injection of acid substances into the veins of a living animal produces instantly coagulation of the blood, and on the other hand, that the blood becomes dissolved on the contrary, when the injection is made with alkaline substances.* These facts are amongst those which have been in a measure rediscovered by modern observers: and M. Magendie has proved that by effecting in living animals a true dissolution of the blood, by means of an alkaline substance mingled with it, we produce in them several of the symptoms that belong to typhus fever.† Such was this Sylvius Deleboë, whose opinions long exercised so powerful an influence on the theory and practice of medicine; a truly distinguished man, whom the insufficient light of chemistry in its infancy, and of an imperfect method of investigation, led to the most singular illusions, but who had the merit of discovering some truths, of foreseeing a great number, and of forming a body of doctrine, the foundations of which, some one may perhaps seek to reconstruct with more solid and more durable materials. It may be that I deceive myself, but it seems to me that while meditating on these hypotheses of the chemical physicians of the sixteenth century, though we may recognize most generally their futility, the mind is nevertheless arrested and returns to them, as though conscious that they place it upon a point of view, where important truths are about to be disclosed to it.

I do not pretend to pass in review the numerous authors

come material for interesting works? this it is which attracts so strongly to the study of the works of Sylvius, and of many other of his contemporaries, though we feel that they do no more than propose problems without resolving them.

* Sylvius Deleboe, praxis medica, lib. i, cap. xxxiii, de febribus malignis.—De peste, sectio iii.—Praxeos medicæ appendix, tractatus ii.—De methodo medendi, lib. ii, cap. xxvi.

† Magendie, leçons sur les phénomènes physiques de la vie, passim.

who, before or after Sylvius, sought like him to determine through chemistry the seat and nature of diseases. On this list would appear the most illustrious names, such as those of Van-Helmont, of Willis, of Boerhaave and of his commentator Van-Swieten: so natural did it appear to these men, who followed in other respects such different doctrines, to bring into play, in their theories of disease, the consideration of the principles which the chemistry of their day showed to exist in the human body!*

* To comprehend these authors, we must not deceive ourselves upon the meaning that they attached to the word so often repeated by them of elements or principles; here is the signification given to it by Willis, (de fermentatione, cap. 1):

"Principiorum nomine intelligo haud entia simplicissima et omnino incomposita, sed tantum substantias, in quas veluti partes ultimo sensibiles, res physicæ resolvuntur. Harum combinatione et motu intestino corpora gignuntur et accrescunt; harum mutuo ab invicem discessu et dissolutione alterantur et intereunt."

But besides, the chimiatric doctrines of the three last centuries, would be unintelligible for him who did not know, that in the language of those times, the expressions by which were designated the elements of the bodies then admitted, had a sense totally different from that we give to them at present. For Sylvius, for Willis, as well as for Paracelsus, the words mercury, sulphur, and salt, were employed in a sense altogether metaphorical, as may be seen by the following passage from the chemistry of Sylvius, which I translate literally:

Chemistry, says Sylvius, is nothing more than the separation of compound bodies into their principles: these latter are five in number, to wit: mercury, sulphur, salt, phlegm, and earth.

Mercury is the name given by chemists to *spirit*, because, like mercury, it is volatile. This *spirit* or *mercury* is any subtle or penetrating liquor, as the spirit of rectified wine, or the spirit of salt of nitre. We call that also spirit which disengages itself from bodies in a state of fermentation, but we ought more particularly to confine this term to whatever is volatile in its material, no matter what may be its origin. In this way we find three spirits; an insipid, a sulphurous, and a saline one.

Sulphur is whatever is inflammable; it is sweet or bitter; the first exists in fat and in flesh, the second in absynthium and in bile: there is one sulphur which is volatile, and another which is fixed.

Salt is whatever can be incinerated; it is acrid, sometimes fixed and sometimes volatile; a fixed salt is one, which may four times be exposed to heat without change; a volatile salt is one which when exposed to a slight heat,

Nevertheless, even during their greatest development, these doctrines were not adopted without opposition; they met with numerous and able opponents, amongst whom we find a learned natural philosopher, Robert Boyle,* and a celebrated observer, Thomas Sydenham. The first brought forward doubts on the reality of the existence of the chemical principles admitted by his contemporaries; he demanded that they should verify by experiment so many gratuitous assertions, and in this way made a wide breach in the applications that had been made of them in medicine. The second strongly opposed the physicians, who according more, said he, to speculation, than to practical observation, long sought to explain diseases by the *new inventions of the chemists;* he accepted the aid of chemistry only to enlighten physicians in the preparation of remedies.† The absolute aversion, manifested by Sydenham for every application of chemistry to medical theories, was certainly in him the very natural result of the impression that had been made upon his mind by the hypotheses of the iatrochemists, and particularly by the conclusions that they had deduced from them for the treatment of diseases, a treatment in flagrant opposition to that the power of which

evaporates and is dissipated in the atmosphere, or which, when enclosed, attaches itself to the sides of the alembic or recipient.

Phlegm is any aqueous, insipid fluid, that is unsusceptible of being volatilized by a very strong fire.

An *earth* is a gross, dry substance which has no other quality than that of remaining in this latter condition, no matter to what test we submit it.

Of these five elements, the three first are called active, because upon them depend all the movements of natural bodies; the two last are called passive, because they do not act in themselves, and because they receive from the first the stations they must occupy; Paracelsus and others refuse them the title of elements." *Sylvius de Leboë, de chymia in genere.*

* Robert Boyle, the sceptical chemist, 1661.

† Et sicuti Hippocrates eos reprehendit, qui huic in humanis corporibus speculandis curiositati plus dant quàm observationibus praticis, ... ità pari jure prudens vir quispiam in hoc nostro seculo eos culpare possit, qui existimant artem medicans nullâ re ullâ magis promoveri posse quàm novis chemicorum inventis ..... at si intrà pharmacopiæ limites centineatur chimia, ars est satis quidem laudabilis.—(*Sydenham, tractatus de hydrope.*)

was daily proved to him by a most admirable observation. Thus, this excellent genius was led to disown and deny the truth of a principle, the abuse or improper application of which had too strongly prejudiced him. More recently Bordeu reproduced these attacks of Sydenham against the utility of the application of chemistry to pathogeny.* In this way it happened, in consequence of the reaction which infallibly occurs against the best principles when exaggerated, that medicine, which for two centuries had drawn most of its theories from chemistry, came to reject in an absolute manner all aid from this science, excepting for pharmacology, as Sydenham had desired; an instrument as yet imperfect was badly employed, it was broken. Nevertheless, more impartial than Sydenham or Bordeu, because he had studied more fully, Haller, while assigning limits to chemical investigation, proclaimed it as necessary to the progress of medical doctrines; laying aside hypothesis, he noted with care, in his great physiology, the results of the few experiments that had been made before his time in order to determine the normal and abnormal composition of the blood; he pointed out by this means the true method to be pursued, and wrote this phrase full of meaning: *Non ideo analyses sanguinis utilitate suâ distituuntur, dum sapienter noverimus spes nostras recidere, neque plura docere quam a naturâ discimus.*†

Such were the fruits of the iatrochemical doctrines, and they existed in science but as wrecks, so to speak, when the genius of Lavoisier arose, to give to chemistry a new aspect, and impart to it a certainty until then unknown. Medicine felt its influence, and began anew to search for the cause and seat of diseases in the various principles which a wonderful analysis had just revealed. But the first essays of this kind were most unfortunate, for they had also for support merely pure hypotheses. While adopting the words of Lavoisier's chemistry, physicians took neither its spirit nor its method, and continued to advance

* Bordeu, analyse médicinale du sang.

† Haller, elementa physiologiæ, lib. v. § xxxiv.

as in the time of Paracelsus. In this way was composed the strange nosography published by Baumes, in which, under the titles of calorinèses, oxigénèses, hydrogénèses, azotènèses and phosphorénèses, the professor of Montpellier, divided diseases into five classes, giving to each one of them a name in relation with the principle or element, which he quite gratuitously supposed to produce them by its modifications of quantity or situation.*

Ancient chemistry has surely produced nothing more hypothetical or more extravagant than this singular classification of diseases: it is beside an imprudent, altogether conjectural application of chemical knowledge to the science of the sick man. If this method had been persevered in, the opinion of Sydenham, and Bordeu would certainly have triumphed; happily however some wise spirits perceived all that was unreasonable and dangerous in it. A few years after the discovery of pneumatic chemistry, two chemists, Parmentier and Deyeux, associated themselves for the purpose of discovering by experiment, to what extent the normal principles of the blood are susceptible of change in disease; but their work rested on too small a number of facts to permit us to draw any useful conclusion from it, and it therefore passed by unnoticed; no one at that period pursued the excellent method which they had just pointed out.† On the other hand, the spirit of the physical sciences which began to be introduced into medicine, caused all the uncertainty of the ancient humorism to be felt: they thought now only of combating and destroying it, and, in the eagerness of the reaction which followed, soon arrived at denying completely that the blood could, by its alterations, play a part in the production of disease. The ne-

* Baumes, *Fondements de la science méthodique des maladies*, 4 vol. in 8°. Idem, *Traité sur la vice scrophuleux, disc. prélimin.* Idem, *Essai d'un système chimique de la science de l'homme*, Nismes, 1788.

† Memoir on the blood, in which the following question is answered: to determine by modern chemical discoveries, and by exact experiment, what is the nature of the alteration that the blood undergoes in inflammatory diseases, in putrid febrile diseases, and in scurvy, by citizens Parmentier and Deyeux. This title stated the problem to be resolved in the clearest possible manner.

cessary consequence of this doctrine, was the neglect of all experimental research as to the alterations of the blood, to which they had ceased to attach the least importance. Vainly did Bichat at that period write thus in his general anatomy; *Humoral medicine has been exaggerated without doubt; but it has solid foundations, and in a number of cases we cannot deny that all should be referred to a vice of the humours.** This protest from a man of genius was not listened to by his contemporaries, and if it had been they probably would not at that time, have followed the proper route for discovering and demonstrating this *vice of the humours*, as Bichat expressed himself in language borrowed from his predecessors: for at that epoch the most absolute contempt was generally expressed for the application of chemistry to the research of physiological and pathological facts.

The same occurred as to the study of the blood by the microscope, as had happened as to its study by chemistry.

It was natural indeed that a short time after the discovery of Leeuwenhoeck, men should endeavour to discover what became of the globules of the blood in disease; but instead of devoting themselves with this view to direct observation, they still proceeded by hypotheses; and, as they had explained diseases by alterations that they supposed to occur in the chemical elements of the blood, in the same way, they explained them by certain alterations which they imagined quite as gratuitously to occur in the globules. It is thus that the celebrated theory of the *error loci*, invented by Boerhaave, by which he explained a very great number of morbid phenomena, had its point of departure in the altogether hypothetical idea of the division of the globules into others much smaller, which could normally penetrate only into vessels whose diameter was proportioned to their own.† Another author, Huxham, supposed that, in fever, the globules became altered by too rapid a movement; he supposed beside that, in diseases called

* Anatomie générale, tome 1, considerations préliminaires.

† Van. Swieten commentar. in Herm. Boeerhaavii aphorismos, t. 1, p. 143, *obstructio.*

putrid, these bodies being softened, were torn and broken into small portions, which entering readily into the smallest vascular ramifications, arrived at the open orifices of exhalent vessels, and were thrown out externally; in this way Huxham explained the hemorrhages of putrid fever.* Had this author then seen the globules thus broken and reduced to fragments in the field of the microscope? By no means: but he supposes by a pure intuition of his mind that it ought to be thus, and does not trouble himself to give the slightest experimental proof of so grave an assertion. If Huxham had examined with the microscope the blood of a patient labouring under putrid fever, he would soon have discovered how little foundation there was for his opinion; for he would have found the globules neither torn nor broken, and would have been compelled to renounce his explanation of hemorrhages. But just as we have seen the good sense of the public finally render justice to the hypotheses of iatrochemistry, so the time at length arrived when all the vanity of these systems erected in consequence of the facts discovered by the microscope was to be recognized. Then it was that Bordeu attacked with bitter irony those authors who, said he, *went so far as to see or imagine the globules bursting and falling to pieces, like so many globules of glass; but sensible people,* he adds, *will care little for such puerilities.* All these vain theories disappeared then, but with them unfortunately were dragged into oblivion the facts so full of interest and of promise upon which they had rested for half a century. Physiology and pathology rejected as useless, or dreaded as a source of error, the employment of the microscope; and this instrument was completely abandoned, as chemistry had been before it. The glory of returning by the experimental method, to the microscopic, as it has done to the chemical study of the blood, was reserved for our epoch.

Thus, by turns abandoned and resumed, the idea of seeking the origin of disease in some change of proportion or of

* Essai sur les fièvres, par Jean Huxham, traduction Française, 1 vol. in 12, p. 3 et suiv., p. 68 et suiv.

nature that the elements of organized bodies may have undergone, has advanced with various fortune from the origin of science down to our days; it has more or less swayed the mind first by the ancient doctrine of the elements, then by iatrochemistry and by the microscopic researches of the three last centuries, and finally by the applications that have been made in medicine of the discoveries of pneumatic chemistry. And if, notwithstanding the many fallacies to which it has led, this idea has never been forgotten, if at periods the most diverse, and in spite of the falsity of the doctrines which have often been its fruit, it has continued to seduce and attract the most eminent men, this depends in my opinion, upon the fact that it contains an important truth, to wit, that one of the possible causes of disease, is some change of relation or proportion, which the elementary principles that compose organized bodies under their two forms of solid and liquid, are susceptible of undergoing. Thanks to the progress of organic chemistry, the moment seems to have arrived when more than ever we may hope to place this truth in its full light, by the rigorous employment of experimental methods; and it would afford proof of a culpable ignorance, or of a dangerous scepticism, to refuse to accept the results of the chemical science of our day, because those yielded by another, which had nothing in common with it but the name, had been convicted of insufficiency or of error.

But in order that chemical and microscopic analysis, applied to the study of the blood in disease, may yield results really useful, one condition is indispensable: which is, to acquire previously an accurate knowledge of all the varieties of the physiological condition of the blood. For want of sufficient acquaintance with all the diversities of aspect and composition that the blood may present, without health being interfered with, we might commit continual errors, as I am about to show by some examples.

And first of all we must not infer the composition of the blood of one species of animal by that of another. I have shown in the memoir published upon this subject in connec-

tion with MM. Gavarret and Delafond, the very remarkable differences which exist in this respect in the various species of animals. We have proved in that work, that there are some classes whose blood contains more than double as much fibrine as that of others, and that these differences exist also for the globules. To what false results then should we not arrive, were we to take as our point of departure in diseased animals, the physiological proportions of the globules and fibrine of man, in order to calculate the changes of composition that the blood may have undergone in these animals, as a consequence of disease.

Neither is the healthy appearance of the blood the same in different classes of animals, and that appearance of this fluid which, in man, is the certain expression of a morbid condition, belongs to other beings in their physiological state: such is the case, for example, in regard to the buffed condition of the blood. In man, whenever a true buff, such as I shall describe farther on, occupies the upper portion of the clot, we may with certainty affirm the existence of a state of disease;* and, whatever may have been said about it, this buff never exists in man in a state of health. But mark! it is not the same in other animals, for this assertion would not be tenable with respect to them. Thus, whenever we bleed a horse, and manage so that the blood flows in a continuous stream with a pretty strong jet, into a vessel neither too large nor too flat, we constantly observe the upper part of the clot occupied by a white mass, which resembles perfectly the buff of human blood. This was shown to me by the observations that I made at Alfort with MM. Gavarret and Delafond. This colourless mass constitutes a considerable portion of the clot; in regarding it, one would take it for the perfect inflammatory

* We must distinguish between the true buff of the blood, and those transparent pellicles, or irisations, which have not the same meaning, and which may be found on the upper surface of the clot in the most diverse conditions of health and of disease. I have shown elsewhere (Réponse aux objections dirigées contre les analyses du sang, etc.) the causes which produce these discolorations of the clot.

buff found in a man labouring under intense pneumonia, or acute articular rheumatism. Why then does the buff belong to the physiological condition of the blood of the horse? I shall endeavour after a while to give the reason.

In different individuals of the same species, supposed always to be in a healthy condition, the different elements of the blood may present variations in their quantity, which however always remain within certain limits. There results from this, for each of these elements, a maximum and a minimum above and below which the physiological condition can no longer exist, while that condition is compatible with this maximum and minimum, as well as with all the intermediate proportions.

The average of the fibrine, in human blood, is in the physiological condition, $\frac{3}{1000}$. I have shown elsewhere that the value of this proportion could not be impaired by other numbers that have been given by some experimentalists as representing the normal quantity of the fibrine of the blood. (See answer to objections brought against the analysis of the blood, etc.) In healthy individuals, the fibrine may vibrate about this average, so as to fall to the proportion of 2.5, or to rise to the proportion 3.5, without the physiological state being thereby destroyed. There are some persons even, who, without being sick, may have in their blood nearly 4 in fibrine, or in whom this element may fall as low as 2. But these are, we must admit, maxima and minima very rarely compatible with the physiological condition; they should be regarded as a kind of exceptional proportions which belong only to true idiosyncrasies.

In taking the proportion $\frac{127}{1000}$ as that which represents the average of the globules in human blood, we find, in the physiological condition, as the maximum of the globules the proportion 140, and as minimum the proportion 110. But this maximum 140 is linked with the plethoric condition, which, by development becomes a true morbid state. Force of constitution is the condition of the economy which most contributes to raise the globules towards their maximum, while congeni-

tal or acquired debility is that which lowers them towards the minimum.

The solid materials of the serum, which are composed almost exclusively of albumen, present, above and below their mean 80,* a certain number of proportions which are equally compatible with the preservation of health; but there is likewise for these materials, and consequently for the albumen a certain degree of diminution which I have never met with, without their being at the same time disease.

Independently of the individual constitutions which introduce into these proportions the variations that I have just signalized, there are still, independent of disease, some circumstances which may equally cause these proportions to rise or to fall, without our being able to accuse therefrom any disease. Thus I have shown in my first memoir that emissions of blood and the deprivation of aliment have for constant effect to diminish the amount of the globules, while the fibrine is much less rapidly and necessarily influenced in this way. I have begun some experiments with a view to determine to what point we may succeed in modifying the proportion of the various elements of the blood, by giving to animals a more or less substantial nutriment. These experiments are not yet sufficiently advanced to enable me to make known positively the results: they will be published in a subsequent work, but I have thought proper to mention them here, as entering into the general plan of the researches in which I am engaged.

Happen what may, what I have just said suffices to show how important it is to have determined with some rigour, for the physiological condition, the possible variations of quantity that the different elements of the blood may present, before pursuing these analyses in the pathological condition.

The same is true in regard to the microscopic examination

* Pure albumen constitutes of this mean about 68 or 70. When, in the following portion of this work, I mention this principle, I refer to pure albumen, separated from the organic and inorganic elements to which it is united in the serum; in case this separation have not been made, I shall employ the expression of solid materials of the serum.

of the blood. This examination should be made with much time and care for healthy blood, before we think of studying by the microscope the changes which this fluid may have undergone.

It is for want of having engaged in this preliminary examination of the physiological condition, that so many erroneous assertions have been emitted upon the changes that the condition of disease may produce in the globules. I do not fear to affirm that up to the present time, no one has observed in a positive manner any alteration of form or texture in these little bodies, which can be regarded as the result of a diseased influence, and that all their modifications of appearance which have been described, and others which have been less dwelt upon, result, some from the progressive destruction that they have undergone in proportion to the length of time that they have been removed from the influence of vitality, and others from some circumstances altogether peculiar, which act upon them, but which are not circumstances of disease. These circumstances have not, in my opinion, been properly appreciated: some have considered, for example, as an indication of the destruction of the globules, that granular or raspberry-like appearance which we so often find, sometimes in the blood of subjects, and sometimes even in the recent fluid, examined shortly after it has been extracted from a living vessel. The researches in which I have been engaged upon this subject, do not allow me to accept this opinion. The globules which assume the raspberry-like appearance have not been changed by disease, nor are they globules in one of the phases of their period of destruction.

When we place in the field of the microscope, between two pieces of glass, a drop of blood immediately upon its escape from the vessel, we readily perceive near the globules properly so called, rounded, white corpuscles, $\frac{1}{500}$ of a millimetre in diameter, the existence of which has been proved by all observers. The red globules, which are at first perfectly regular, with abruptly terminated outlines, soon become changed in their exterior shape. Some present upon their surfaces, one,

two, or three little protuberances, and are called raspberry-like; others, resembling iron cog-wheels, seem regularly festooned and cut upon their edges. So long as the desiccation of the drop of blood is not complete, the number of red globules thus deformed augments in proportion to the length of time from the commencement of the experiment. As to the white corpuscles, they become more rare as the preceding alteration advances and becomes general.

The rapidity of formation of the kind of nipples or protuberances which stud the red globules, and the important fact that their exterior aspect and dimensions are absolutely the same as those of the white corpuscles, all led me to think that this deterioration of the globules was due to a simple attachment of the white corpuscles which surrounded them. By following attentively all the movements of displacement which occur in the field of the microscope, I have been enabled to witness the production of the phenomena, to see the white corpuscles approach the red globules, dispose themselves upon their surfaces, adhere to their edges, and in this way to form every possible variety of the raspberry-like and festooned globules. This mamelonated appearance, which some have regarded as the commencement of their destruction, and others as the result of a pathological influence, is but the result when strictly examined of the precipitation of the white corpuscles upon and around the red globules.

But what is the nature of these white corpuscles? Here a general fact is about to appear. Whenever we examine blood as it escapes from the vessels, we establish first the presence of isolated white corpuscles, and afterwards the raspberry-like and festooned appearance of a certain number of red globules. When, on the contrary, we, in any way, deprive the blood of all its fibrine, before spontaneous coagulation, we no longer find white corpuscles in the field of the microscope, and the red globules present neither the raspberry-like, nor the festooned appearance. When left a long time to themselves, these globules, thus separated from the fibrine, diminish gradually in size, become reduced to a kind of central nucleus, and finish

by disappearing entirely, but in no case are either their surfaces or their edges studded with prominences. The presence of fibrine then is necessary in order that the drop of blood should contain white corpuscles, and without these the alteration of the globules is not produced.

The fibrine may likewise be studied under the microscope before it has spontaneously concreted into thick and resisting membrane, in that semi-transparent and seemingly oleaginous layer, known under the name of liquid buff, which constantly and normally forms on the surface of blood drawn from the horse, and only in well-determined pathological conditions in man. This fluid buff, it is well known, is nothing more than serum holding in suspension an enormous quantity of fibrine, and this latter principle presents itself in the form of white corpuscles of the same exterior aspect and dimensions as those of blood not deprived of fibrine. In order to study the fibrine before its complete coagulation with yet greater ease, it is only necessary to mix some blood as it escapes from the vein with one-seventh its volume of a saturated solution of sulphate of soda. The mixture rapidly divides into two portions, one below consisting of perfectly unaltered globules; the other above, formed of an opaline fluid, where the whole of the fibrine is held in suspension, under the form of white corpuscles $\frac{1}{300}$th of a millimetre in diameter, as in the fluid buff. The solidification of the fibrine goes on very slowly, and one can readily trace the different phases through which it passes, while changing from the liquid to the solid state.

If we take a drop of blood deprived of fibrine, the globules of which are in consequence perfectly pure, and can no longer undergo the change known under the name of the raspberry-like and festooned appearance, and add to it some fibrine in the condition of corpuscles prepared with the sulphate of soda, or taken directly from the fluid buff, we see reproduced all the phenomena of which I have spoken, in regard to blood not previously deprived of its spontaneously coagulable element.

This granted, it is very easy to understand what happens when we place a drop of blood on a plate of glass, and blow

strongly upon it, in such a way as to spread it out into an extremely thin layer. If the operation be well done and with rapidity, the globules remain perfectly unchanged, their surfaces are smooth, their edges very cleanly cut, and left to themselves, they never become either raspberry-like or festooned. In these circumstances the evaporation of the serum is almost instantaneous, its solidification, so to speak, immediate, and the fibrine has not time, as in the case where the blood is placed between two plates of glass, to oscillate about the red globules under the form of white corpuscles, and deposit themselves on their surfaces and edges. Let no one object that the raspberry-like appearance assumed by the globules inclosed between two glasses depends on the fact of their being altered by the compression; for, if we place a drop of blood entirely deprived of fibrine between two glasses, we never see the globules become surrounded by granulations. And if moreover I have dilated in this place upon such a subject, it is in order to show, by this example chosen from many others, how important it is to investigate with minuteness all the influences that can take from the globules their normal aspect, before considering these changes as the product of a pathological influence. What beside more diversified than all the variations of form that the globules may take from their simple contact, or than the figures they may assume by their agglomeration, without our being able to accuse disease of having given origin to such changes?

When we shall in this way have studied sufficiently all the influences which, foreign to disease, may produce in the blood changes in its physical properties, in its chemical composition, and in its microscopic constitution, it will become possible to investigate the alterations that it may undergo, in these different respects, by the fact even of disease. It is of this that I am about to treat in the following chapter.

CHAPTER II.

OF THE BLOOD IN DISEASES.

I HAVE pointed out in the preceding chapter, the methods which it is most convenient to follow, and the preliminary researches to which it is indispensable to attend, in order to study with advantage the alterations that the blood is susceptible of undergoing in diseases.

The alterations that chemical analysis and microscopic examination enable us to trace in the blood ought, it seems to me, to be divided into three great classes.

In a first class, I range the alterations of the blood which result from the fact that the principles which enter normally into the composition of that fluid do not exist there in the proportion compatible with the physiological condition.

The normal elements of the blood, in which the present state of our knowledge enables us to trace these changes of proportion, are the globules, the fibrine, the albumen of the serum, the different organic materials other than the albumen, which are found in the serum, (fatty matter and others,) then the inorganic principles contained in the blood, and in particular the free alkali which it contains, its different salts, and its water.

But this is not all; and here the idea presents itself of inquiring whether disease, in some of its manifestations, may not have the power of rendering more abundant, and consequently more appreciable by analysis, certain materials of the secretions which we may suppose to exist naturally in the blood, but in too small quantity to make it possible for us to discover them in its normal condition. Disease would furnish then the means of recognizing them, by increasing their proportion, as it sometimes makes more apparent also certain tissues, by causing them to emerge from their rudimentary state.

Microscopic researches should not often be employed in the study of this first class of alterations; it is not indeed by such means, as some persons have supposed, that we can even determine an augmentation or diminution of the number of globules.

Without being changed in quantity, the normal principles of the blood may become modified in relation to their size and their physical properties. The microscope may, for example, disclose differences in the volume or in the form of the globules, etc. Here we have a second class of alterations.

Finally it may happen, that in the place of, or in connection with the normal elements of the blood, there may be formed new principles which have no analogues in the healthy condition, and which may be compared in that fluid to what the accidental formations are in the solids. Here then is a third class of alterations of the blood, for the discovery of which should co-operate both chemical and microscopic researches. It is the microscope, for example, which will reveal to us the presence of pus in the blood, etc.

I am as yet far from being able to trace a history even incorrect, of all these alterations; but such is the circle which I have determined to pursue, by following out the modes of investigation, whose value I have estimated in the preceding chapter.

It was proper for me to commence with the study of the alterations comprised in the first class; and in this class, the normal elements of the blood, whose changes of proportion in diseases I have sought to appreciate, are still only the globules, the fibrine, the solid matters* of the serum, and the water. I am about to exhibit, in the following articles, the results that I have obtained, and I shall strive to show how, in each disease, the changes of proportion that the blood may have undergone

* In the memoirs which I have already published, I had estimated in mass the quantity of these solid materials. More recently I have endeavoured to separate them one from the other, so that I might indicate with greater precision for certain cases, the variations in proportion of the albumen properly so called, contained in the serum.

in its physical properties are in relation to its changes of composition, and are explicable by them.

Besides, the analysis of the blood in the diseased condition reveals such great differences in the composition of this fluid, that it is difficult not to admit *a priori* that changes so remarkable in the relative or absolute proportion of its constituent principles must exercise a strong influence upon the organism, and intervene as cause in the production of a more or less considerable number of diseases. When for example, we see in the morbid condition that the composition of the blood, varies to such an extent that instead of a thousand parts, there may be only seventy-five of solids, or even only seventy, we cannot understand that so enormous a difference in the quantity of the elements held in suspension or in solution in the water of the serum should not be taken into serious consideration in pathogenic theories. This it is which I shall endeavour to bring out in what is about to follow.

I shall begin by showing what are the modifications produced in the composition of the blood by two states of the organism, which, when to slight extent may still coincide with health; which, when to a greater extent, cease to belong to the physiological condition, and which, in a great number of cases, complicate diseases and modify their symptoms. These two states are on the one hand plethora, and on the other anæmia.

ARTICLE I.

Of the Blood in Plethora.

True plethora is more frequently constitutional than acquired: we cannot always create it at will by the use of a very substantial aliment. It is not sufficient, in order to produce it, that an individual shall introduce daily into his digestive organs, a large quantity of reparative material, and that

he shall expend very little. Plethora seems to depend often upon a primordial constitution of the blood, which it is impossible for us to produce so readily as we can produce anæmia, that is to say, in other words, that it is much more in our power to impoverish the blood than to increase its richness.

In plethora, as in anæmia, the peculiar state of the blood is the appreciable cause of the general modification which the organism presents. This is for us at least the primitive fact beyond which we cannot go, and to which we have the right to refer all the others. Beyond a doubt some forces have been in action in the naturally plethoric or anæmic individual, from the commencement of the formation of the being, which have impresssed upon the blood a certain constitution that it is ordained to preserve; but this constitution, once produced, does not the less remain the single demonstrable fact, the only one that observation can seize upon, in order to make of it the *experimental cause* of the phenomena.

But are the limits of the science established when it has been said in a general manner that the blood is abundant and rich in plethora, that it is thin and impoverished in anæmia?—This question it is important to examine, and I proceed by turns to occupy myself in resolving it for both of these conditions.

The most accredited opinion relative to the state of the blood in plethora, is, that it fills the vessels in very large quantity, that its different organic elements have become more abundant, and that it is in particular richer in fibrine.

Let us examine one after another these different assertions.

It is impossible to demonstrate the augmentation in quantity of the blood in plethora—how estimate in reality what is in weight or in volume the mass of fluid contained in the vessels?

But if we cannot arrive at this valuation, and if, in consequence, we are compelled to acknowledge our ignorance as to whether plethoric persons have in their circulatory apparatus

more or less blood than other individuals, we can seek to determine whether the blood of such persons has not a peculiar constitution. Now, with respect to this, here is what analysis has taught me:

It has shown me in the first place that it is not true that, in plethora, the blood contains very much more fibrine than in any other condition; I have found, in reality, 2.7 of fibrine, as the average of this principle, in thirty-one bleedings performed upon individuals in whom the plethora was fully characterized. Some presented as yet no marked symptoms: in them the bleedings were simple measures of precaution; in the others, were observed vertigo, tinnitus aurium, palpitations of the heart, excessive difficulty of respiration, an injection as though apoplectic of the conjunctivæ of the eyes, and of the face, etc. Thus, in these individuals, the fibrine did not even quite equal the physiological mean. The symptoms of plethora do not depend then, as has often been repeated, upon an augmentation of fibrine in the blood. Consequently, in the point of view of the composition of the blood, plethoric individuals should not be more disposed than others to contract inflammations, and I do not fear to affirm that, if clinical facts be interrogated as to this, they will lead to the same conclusion; it is but a false analogy of symptoms which has caused it to be said that plethora disposed to the phlegmasiæ. The results yielded by the analysis of the blood are found here to be in perfect accordance with those to which clinical observation conducts.

The fibrine does not then sensibly augment in plethora; it remains within the limits of its physiological state, and does not even tend, in the greater number of cases, to mount towards the higher limit of this state.

The organic materials of the serum do not offer either, in plethora, any remarkable change of proportions.

The globules alone remain, and it is effectively the great elevation of their proportion which establishes in the blood the character of plethora; in the 31 bleedings to which I have

already referred, I found for the mean of the globules the cipher 141; for minimum, 131; and for maximum, 154.

The blood of plethoric persons then differs from ordinary blood in the greater quantity of globules and the much less quantity of water that it contains.

The physical properties of this blood may be perfectly explained by the nature of the changes that it has undergone in its composition.

Thus, before coagulation, the blood of plethoric people is remarkable for its high coloration, which is in relation with the large proportion of globules it contains.

When we examine it after coagulation, we observe generally that the serum is more or less coloured, that the clot is large, voluminous, of moderate firmness, and that it retains a large quantity of serum; we never find any buff upon its surface; at most we may sometimes observe there a thin and transparent pellicle, or some scattered irisations, if the blood has flowed very rapidly from the vein.

The considerable volume of the clot depends manifestly upon the large number of globules, and its softness, as well as the constant absence of the buff, depends upon the small proportion of the fibrine relatively to that of the globules.

The excess of globules in the blood of plethoric people coincides in them with a certain modification of the physiological state, and also with a certain number of pathological facts which seem to be a consequence of it.

Thus, all the functions are usually more active, and there is as it were an exuberance of life: digestion proceeds rapidly; respiration is favoured by the great development of the thoracic cavity; the circulation is rapid, the heart beats with force; but it is an error to admit, as has been done, that in such cases, its pulsations may be accompanied by a bellows-sound. I myself not long since put forth this opinion; but a more attentive and a longer observation have convinced me that it is not so, and that consequently, in those cases where a bellows-sound had been heard in the heart or arteries of plethoric patients, it is because the diagnosis had been badly made

and because there had been some other disease with the plethora.

While dwelling on all these modifications of functions which coincide with the plethoric condition, I do not wish to repeat here what is everywhere known; it was only necessary for me to speak of them, in order to make evident their coincidence with the fundamental modification that the blood undergoes in that condition, to wit, an augmentation of its globules: however I will remark besides the peculiar disposition that the brain then presents to become excited, the facility and at the same time the mobility of the emotions, without our observing at the same time those exaggerations or those aberrations of sensibility, and those nervous predominances, which we shall presently find to accompany almost necessarily an opposite state of the blood, to wit, the anormal diminution of its globules.

The individuals whose blood contains an excess of globules are subject to some peculiar symptoms, of which no one has perhaps up to the present time given a very satisfactory explanation; thus, the vertigo, the dizziness, the tinnitus aurium, the heat of head that they experience, have been accounted for by congestions of blood towards the brain; but these congestions have never been, in like conditions, anatomically proved, and the mere passage of an excessive quantity of globules through the vessels of the brain appears to me a fact sufficient to account for them; but, singular circumstance, if it happens on the contrary that too small a number of globules traverse these same vessels, analogous symptoms will still present themselves, so that a quantity of globules either too high or too low disturbs in the same way certain cerebral acts.

An excess of globules in the blood coincides also with the more frequent and more ready appearance of certain hemorrhages; I shall endeavour further on to give an explanation of this.

Finally, in these cases of excess of the globules, it is not uncommon to see arise by intervals, a general increase of excita-

bility of the organism, carried to such a point that a true fever may be the consequence. Vainly should we seek, in order to account for this, any alteration of the solids; they do not present any, and the fever ought then to be considered as having its point of departure in some state of the blood. But, let us take another case: suppose that coincidently with some inflammatory alteration of a solid, developed in an individual whose blood contains too many globules, there arises fever; this will then present a physiognomy altogether peculiar; it will be remarkable by the symptoms of high reaction which shall accompany it; it will present that type of fever called by Pinel angeiotenic; and this type will depend less upon the seat and nature of the local lesion, than on the condition of the blood itself. Venesection will certainly modify it, by acting on the blood, whose globules it will infalliby diminish; but though evidently useful in this point of view, it will have a much less direct influence on the inflammatory alteration which has produced the fever; for this alteration is connected with another modification of the blood, upon which bleeding has much less direct and immediate influence, as we shall see further on.

The phenomena of plethora, viewed in connection with the composition of the blood in this condition, may enlighten us on the part played by the globules of the blood in the organism.

ARTICLE II.

Of the Blood in Anæmia.

I HAVE just pointed out what may result in the organism, in the state of health and of disease, from an excess of the globular element of the blood. But there are cases also in which this fluid comes to present a character precisely inverse, that is to say when its amount of globules falls much below the physiological mean, and diminishing more and more,

reaches a proportion so low that we can scarcely comprehend how, with so few globules in the blood, life can still be maintained.

This diminution, in different degrees, of the globular element of the blood is the fundamental character of anæmia, a condition which, therefore, in regard to the composition of the sanguine fluid, as well as in relation to its symptoms, is the opposite of plethora. According to the degree of the diminution of the globules, this condition is still compatible with a certain amount of health, or it becomes by itself a true morbid state, which may exist alone, or intervene as complication in all diseases. Thus then, independent of the solids, we find one of the principles of the blood, becoming distinct from all the others, exercising, sometimes by its augmentation, and sometimes by its spontaneous diminution, an influence such as to become the point of departure and the sole appreciable material element of a considerable number of diseases.

I have found, as the average of the proportion of the globules, in 16 cases of commencing anæmia, the cipher 109, and in 24 cases of confirmed anæmia, the cipher 65. I have constructed these averages only from cases of spontaneous anæmia occurring in the human race; I should have found a lower average in the sheep kind, which are also exposed to become anæmic, and which, in this condition, may have a blood so deficient in globules, that I have seen one of them which had but 15 of those corpuscles (see Memoir, etc.), whilst in the human race, the lowest proportion of globules that I have ever met with in spontaneous anæmia is 28. It is true that man possesses normally in his blood more of the globules than does the sheep species; whence it follows that, proportionally to the physiological condition, the minimum 28 of globules, found in the spontaneous anæmia of man, is very nearly equal to the minimum 15 found in anæmic sheep.

Besides, it is necessary to distinguish several kinds of anæmia, according to the modifications of composition that they produce in the blood.

In spontaneous anæmia, whether strongly marked or not,

the globules alone are diminished: the fibrine and the solid matter of the serum have preserved their normal proportions; thus in 16 cases of slight anæmia, I have found as the average of fibrine the cipher 3.0; and in 24 cases of confirmed anæmia the cipher 3.3.*

In the anæmia which follows more or less abundant losses of blood, it may equally happen that we shall find the globules alone diminished; that is indeed the first effect of every hemorrhage; but if this augments or is renewed, there soon arrives a moment when the blood comes to lose equally its other principles, and we see the albumen and the fibrine of the serum diminish with the globules. It is in this way that in a woman who had suffered from very abundant attacks of metrorrhagia, the blood contained only 21 in globules, 1.8 in fibrine, and 61 of solid matter of the serum. The water had risen to the enormous proportion of 915.

Anæmia may also be the result of certain appreciable modifications of the organism which exercise an influence on the blood. In this case, the composition of that fluid appears to be the same as in spontaneous anæmia, that is to say the globules alone are diminished, while the fibrine and albumen of the serum remain the same. This is what occurs in many pregnant women whose blood loses its globules without losing its fibrine. The average of the globules is the same in them as we have found it in cases of slight anæmia.

Why is it that woman is more exposed than man to this singular alteration of the blood in virtue of which, without

* The state of the blood of animals shows perfectly to what point the fibrine and the globules may remain isolated in their increase or diminution; thus, the dog whose blood contains much less fibrine than that of man and of all other animals that I have examined, is precisely the animal whose blood is most rich in globules. On the contrary the horse, the sheep, the ox, whose blood contains more fibrine than that of man, and especially than that of the dog, have in their blood much less of globules than the two other beings.—(See the *Memoire sur la composition du sang de quelques animaux domestiques, etc.*) Besides, in the same species, those individuals who possess in their blood the most globules are not those whose proportion of fibrine necessarily rises highest, and *vice versâ*.

any evident cause, the globules of this fluid are thus diminished in so strong a proportion? Why is she particularly exposed to it at a certain epoch of her life?

Yet men also are sometimes attacked with spontaneous anæmia; they present in such a case all the symptoms which characterize the chlorosis of the female, and I have proved that their blood then suffers the same alteration of composition; it is with them equally the globules alone which diminish; the fibrine and the solid matter of the serum remain the same. I have met with examples of this spontaneous diminution of the globules both in men still young, and in others aged from forty to sixty years.

When the influence of lead has acted for a long time upon the human constitution, there may result from it the production of a cachectic condition, very well described by Doctor Tanquerel; I have found that, in this condition, the globules of the blood suffer as great a diminution as in spontaneous anæmia, and, as in this latter, the fibrine and other elements of the blood preserve their normal quantity. This effect of the saturnine intoxication repeated or prolonged is certainly very remarkable.

It would be very curious to know whether the globules at the same time that they are diminished in quantity in anæmia, do not become altered also in their structure, and tend to undergo a true destruction. I announced in my course at the Faculté in 1840–41, the results that some microscopic researches undertaken with this view have yielded me. It seemed to me, in two cases of chlorosis, that the globules were become smaller than we generally see them, and at the same time a certain number had no longer their accustomed form; they appeared in the field of the microscope, as though broken, and disseminated, like kinds of fragments. A young girl who presented me this singular condition of the globules, on the 6th of December, 1840, was perfectly cured two months later; her constitution had even undergone such a metamorphosis, that it had gradually arrived under our own observation at a plethoric condition; the 14th February 1841, I was obliged to

bleed her, and her blood then presented me very beautiful globules, extremely different from those that I had observed in December.

These facts seem to me of so much interest and importance as to make me feel the necessity of seeing them again, before accepting them definitely, and drawing deductions from them.

The physical properties of the blood in anæmia are very well accounted for by the nature of the changes that it has undergone as to its composition.

In the most ordinary condition, the one in which the only change undergone, consists in a diminution of its globules, the blood presents to the naked eye the following appearance:

Supposing it to have flowed freely, we find in the vessel which has received it a small clot which swims in the midst of an abundant and perfectly colourless serosity. This clot, far from being soft, as we might have expected, is on the contrary remarkable for its density; its molecules retain a strong power of cohesion, and it is not at all uncommon to find upon its surface a very characteristic buff; one might take it for pleuritic blood, or for that of an acute articular rheumatism. This density of the clot, and the buff which covers it, are the more marked in proportion as the anæmia is more considerable. The existence of cupped blood in anæmia is not a new fact in science. Borsieri, amongst others, had noticed the presence of the buff in the blood of chlorotic patients, and he had with good reason, drawn from this an argument against those who pretended that this crust was always the necessary indication of a phlegmasia; and it is curious to find that Tommasini, who had also seen the coagulum of the blood of chlorotic patients become covered with a buffy coat, would not for that abandon the principle sustained by him, that there is no buff in the blood without inflammation; for, said he, chlorosis is nothing more than a chronic angioïtis. Such an assertion does not even require refutation.*

* Tommasini sull' inflammazione, t. 11, p. 250 to 278.

I regard as incontestable, the fact that the clot of the blood of chlorotic patients is often buffed, and like Borsieri, I have from this long since drawn the inference that the presence of the buff is not always evidence of the existence of an inflammatory disease, for chlorosis is certainly not of this character. But why is the blood, in this disease, often cupped? It is because the blood of chlorotic patients has retained all its fibrine, and lost some of its globules; it is in consequence of this that there is really in this blood, as in that of inflammations, or as exists normally in the blood of some animals, excess of fibrine in proportion to the globules; now, whenever this excess takes place, whether it be absolute or relative, and whenever at the same time the coagulation of the fibrine is not very much too rapid, this principle will be seen to accumulate alone on the surface of the clot, and the cup will appear. This is the reason why the blood of anæmic individuals may be buffed, and why that of plethoric individuals is not; it is the cause also why the coagulum of blood is firmer and more dense in the first than in the last. It is also one of the circumstances which explains the constant existence of the buff in the blood of the horse. We must add to this, in the latter animal, the greater slowness of the coagulation of the fibrine.

Thus, all those various functional disorders which accompany anæmia correspond to an alteration of the blood which is always the same, to wit, a diminution of the globules, and the intensity of these disorders is so much the greater in proportion as the globules have themselves undergone a more considerable diminution of their cipher. If this diminution be slight, it is compatible with the persistence of a certain physiological condition; if it becomes rather greater, the disease commences. Whatever indeed be the cause that may have brought on diminution of the globules, the resulting symptoms differ only in relation to their degree of development; but remain the same as to their nature. Whenever we find the diminution of the globules to coincide with that of the albumen, or with that of the albumen of the serum, we shall observe peculiar symptoms appear, which I purpose mentioning

further on; so that what I am about to say at present will regard only the most common case of all, that in which the anæmia is the simple manifestation of a diminution of the globules alone.

The blood cannot be deprived of a certain quantity of its globules, without there resulting from it great prostration of the muscular system, very marked general feebleness, grave perturbations of the nervous system, which are betrayed by different disorders of the intelligence, of sensation and of motion; and various disorders of the functions of digestion, respiration and circulation. Who is ignorant of the various neuroses to which anæmic patients are subject, their dyspepsia, their dyspnœa, their palpitations of the heart? Who has not observed the singular discoloration of their skin and exterior mucous membranes, which is so naturally explained by the small number of colouring globules which still flow in their vessels? But what is less generally known is, that it is not uncommon to meet with individuals whose colour remains natural, whose cheeks even are habitually injected to a remarkable extent, and whose external aspect would easily make us regard them as of a plethoric habit, but who nevertheless have in their blood, an insufficient quantity of globules; this is because there exists in them a false appearance of plethora. Observe in effect such individuals a little more closely, and you will be struck with their feebleness; they will have, as in the most advanced anæmia, vertigo, dyspnœa, and palpitations, upon the slightest effort; they will bear with difficulty any kind of exertion, and still worse venesection, which far from diminishing, will increase their symptoms. All this shows that the diminution of the globules of the blood, before betraying itself by the discoloration of the cutaneous tissue, may declare its existence by the perturbation which it produces in the different vital acts, and this perturbation is always marked by symptoms perfectly identical.

There is a phenomenon revealed to us by auscultation, which constantly coincides with a certain diminution of the globules; this is the singular bellows-sound, heard in the heart,

and especially in the arteries, in all cases of anæmia however slight. For its manifestation, it is necessary that the impoverishment of the blood should have fallen upon the globules; it is not present when the fibrine alone has been diminished; so that I have never met with it in scorbutic patients, unless they had reached that period at which the globules, at first unaffected, yield in their turn. Neither have I met with this *bruit de souffle*, in the cases which will be detailed farther on, where the impoverishment of the blood is owing particularly to a diminution of the albumen of the serum. Remark in addition, what the analysis of 88 cases in which this bruit existed in the carotid arteries, either continuously or intermittently, has taught me, in regard to the relation to establish between the diminution of the globules of the blood, and the appearance of the bellows-sound in the arteries.

Of these 88 cases, there were 56 in which the souffle was continuous, and 32 in which it was intermittent.

Of the 56 cases in which the *bruit de souffle* was continuous, and represented what M. Bouillaud has called the *bruit de diable*, I found 28 in which the cipher of the globules had not risen above 80, and had fallen even to 21; I found 13 in which the cipher varied between 80 and 100; 10 where it had risen from 100 to 115; and 5 again where from 115 it had increased even up to 125.

Of the 32 cases in which the *bruit de souffle* was merely intermittent, there were only 3 below 80 in globules (76, 77, 77); 13, from 80 to 100; 8, from 100 to 115; 8 others from 115 to 126.

We see then that the *bruit de souffle* of the arteries does not always show itself with the same degree of diminution of the cipher of the globules, in different individuals; there are nevertheless some rules to be established in regard to this, such as the following:

1. When the globules are so much diminished as to be below the cipher 80, the *bruit de souffle* exists in the arteries as a constant condition. I have not found a single exception to this law.

2. When the globules remain above this cipher 80, the *bruit de souffle* may still show itself, but it is no longer constant: we continue to hear it not unfrequently, while the cipher of the globules oscillates between 80 and 100; it is still heard, but much less frequently, in proportion as the cipher of the globules passes 100, and finally is no longer observed, at least as dependent upon an alteration of the blood, when the cipher of the globules has risen above its physiological mean.

Whatever be in other respects the nature of the disease in which the diminution of the globules exist, the *bruit de souffle* of the carotids does not the less show itself; I have verified it in the most opposite cases, in putrid fevers, in eruptive fevers, pneumonia, acute articular rheumatism, and in a great number of chronic diseases. But in all these cases it occurred only in connection with the ciphers of the globules above indicated.

The *bruit de souffle* shows itself sufficiently often in pregnant women, which is in relation with the frequent diminution that the globules undergo in them.

The intensity of the bellows-sound, is commonly subordinate to the degree of diminution of the cipher of the globules.

Thus in 22 cases of chlorosis, I have found the intermittent souffle 8 times, the cipher of the globules oscillating between 117 and 77, and the continuous souffle 14 times, the cipher of the globules varying from 113 to 28.

I have sought to find as to what extent the diminution of the globules exercised an influence upon the temperature of the living body, but have arrived in this respect at results merely negative. I have been not a little surprised to observe this temperature remain normal, even in cases where the globules had undergone the most considerable diminution of their cipher. It is thus that individuals who had in their blood no more than 50, 40, 30 and even 21 parts in globules for 1,000 parts of blood, preserved nevertheless in the axilla a temperature which varied between 37 and 38° centigrade: is not this the temperature which belongs to the greater part of men in health? And not only does the temperature not fall because

the globules diminish, but we see it even rise, notwithstanding this diminution, as always happens, when anæmic persons are attacked with fever; for they are exposed to this like other individuals.

We must not then forget that at the commencement of every disease, the blood may present two great modifications in its globules, one of which belongs to plethora, and the other to anæmia. It is upon a variation of increase or diminution in the cipher of the globules that depend the peculiar symptoms then observed, and which are superadded to those of the disease.

ARTICLE III.

Of the Blood in the Pyrexiæ.

The pyrexiæ form a large class of acute diseases which it has vainly been sought to dismiss from nosological systems, in order to throw them all into the order of simple inflammations. Such pretensions however cannot be maintained: the pyrexiæ exist as diseases apart; the causes which often develope them, the symptoms which characterize them, the special nature of the alterations that they produce in the solids, the epoch of development of these alterations often posterior to that of the febrile movement, here are already enough of grave reasons for not confounding the pyrexiæ and the phlegmasiæ; but the analysis of the blood comes still more to establish a very remarkable difference between the one and the other class; the results furnished by this analysis have something so marked, that they seem to me to fix in a definite manner the distinction, vainly combated, between the pyrexiæ and the phlegmasiæ; this is what I am about to endeavour to prove.

Whilst, in the phlegmasiæ, there are always two constant alterations which march together, that of a solid, and that of the blood, it is no longer the same in the pyrexiæ; in these diseases in reality, the only phenomenon which never fails, is

the fever itself; the various alterations of which the solids are the seat, may be entirely wanting, nor do the changes of composition that analysis has discovered in the blood appear in all cases; so that, in the present condition of our knowledge, the character of the pyrexiæ still remains a negative one; that is to say, that, until more fully inquired into, the fever, which accompanies the pyrexiæ, recognizes neither in the solids, nor in the blood, any constant alteration that can account for it. Nevertheless, we can more or less frequently, find alterations in the blood and in the solids; yet these are but the effects of a more hidden cause which governs the constitution, effects however which it is important to study thoroughly, since in their turn they themselves become causes of a certain number of symptoms, and because by their seat and by their nature, they serve to classify and denominate the pyrexiæ.

In my first memoir upon the alterations of the blood, I have proved that, the fibrine never augments in the pyrexiæ, supposing them divested of all phlegmasial complication; that it often remains in normal quantity, and that sometimes it diminishes to a point at which we do not find it in any other acute disease. I have shown that the pustules of variola, and the dothinenteric plaques of typhoid fever, do not have the power of increasing the cipher of the fibrine; and finally I have shown that with all the possible proportions of the globules, whether they were very abundant, or whether they have become very rare, a pyrexia could equally arise with all its varieties of form and gravity.

But is it indifferently, and as it were by chance, that the fibrine shows itself, in the pyrexiæ, either in normal quantity, or in a proportion infinitely more feeble than in the physiological condition? No, without doubt, and with regard to this, very clear general principles may be laid down.

At every period of clinical observation, and upon whatever theoretical point of view, the observer was placed, it has been recognized that amongst the pyrexiæ, there were some unattended by any grave symptoms, which marched naturally towards a favourable termination; while there were others which, either

at their commencement, or during their course, were accompanied by accidents of such a nature, that it seemed as though the forces which rule the organism were either vanquished, or profoundly disordered to such an extent that the extinction of life must be the consequence; and at the same time it was found that in such cases the blood presented an altogether peculiar appearance; it was observed that, become less consistent, it seemed to tend towards a sort of dissolution. Admitted at all periods, but differently explained according to the prevailing theories, this condition which may develope itself in any pyrexia, and towards which several seem to tend naturally, has been called turn by turn putrid, adynamic and typhoid state; it has its greatest development in the typhus fevers properly so called; it is in some sort inherent in them; it is as it were their essence. The pyrexia now called typhoid fever, presents it in a slight degree from the invasion and the grave cases of this disease are its marked representation. It does not ordinarily exist in the eruptive fevers, but it often complicates them, and constitutes one of their dangers. Finally, in addition to the pyrexiæ with well marked characters, and which have a fully determined place in nosological systems, there are others to which no name has been given, which may yet present in a high degree the different symptoms to which the ancients attached the idea of the putrid state. This is because there may exist in effect, in all the pyrexiæ, a common alteration of which the blood is the seat, and whose existence constantly coincides with the appearance of those phenomena always the same, attributed by vitalism to adynamia, by solidism to relaxation of the fibre, and by humorism to putridity of the humours. This alteration of the blood consists of a diminution of its fibrine; it is consequently an alteration the inverse of that which betrays in the blood the phlegmasial condition.

This diminution of fibrine, every time that it takes place, produces remarkable modifications in the physical qualities of the blood. Whatever be the pyrexia in which it exists, blood drawn from a vein presents the following condition:

The serum and the clot are imperfectly separated from each other, whence it follows that there seems to be but little serum in proportion to the clot.

The clot is voluminous, it often fills the whole breadth of the vessel in which the blood has been received; it is never elevated upon its borders, as is so commonly the case with the clot of the phlegmasiæ. Its consistence is always slight, it is torn and broken with the greatest facility, and there are some cases even where, by the slightest pressure, it may be reduced to a true condition of diffluence; it ceases then to form a single mass, and is divided into a number of grumous portions which mix with the serum, and colour it of a more or less deep red. This is the condition of dissolution of the blood so well described by the ancients, and which ought to be regarded as the necessary consequence of the diminution that the spontaneously coagulable matter of this fluid has undergone. Then, in effect, the net-work, which maintained the globules pressed one against the other, and which by its power of contraction squeezed out the serum, no longer exists but imperfectly; thence also arises the great size of the clot, which is found to be in an inverse proportion to its density, and which is not a certain index of the quantity of solid material that it contains. Let us add however that the cause of the large size of the clot, is really also the large proportion of globules that it contains, especially in the early stages of the disease; for these do not diminish in such cases, like the fibrine; far from that, they may become remarkable by their abundance. Very frequently, indeed, I have been struck by the great elevation of the cipher of the globules in individuals with grave typhoid fever; and in my first memoir upon the alterations of the blood, I was even inclined to suppose that this superabundant quantity of globules was one of the characters of that fluid in the pyrexiæ; but this was because I had not then sufficiently studied the condition of the blood in the plethoric; since then I have convinced myself, that if, in typhoid fever, we often find this predominance of the globular element of the blood, it depends on the fact that typhoid fever most frequently attacks

individuals, who by their age and constitution, are in a condition of plethora more or less marked; but the superabundance of the globules depends so little upon the typhoid fever itself, that this disease, as I have myself seen, may occur in chlorotic girls, whose blood is so poor in globules. But whether these be abundant or not, the influence of the disease upon the fibrine remains always the same.

There is another quite negative character of the blood in the pyrexiæ, which is of importance and which serves still more to distinguish the sanguine fluid of these diseases from that of the phlegmasiæ. This character is the absence of the buff. I may affirm here that I have never met with it, unless there was some phlegmasial complication, either in inflammatory fever, in slight or severe typhoid fever, in measles, in scarlatina, or in variola.

Nevertheless, we may find the buff upon the surface of the clot, in this latter pyrexia, when the eruption is very confluent, and especially when collections of pus exist beneath the skin, or in some organ; but this buff always appeared to me to have a peculiar aspect; far from being firm and consistent, like the ordinary crust of the phlegmasiæ, it is very soft, and gelatinous as it were, and however thick it may at first appear, may be rapidly changed into quite a thin pellicle, by expelling by means of compression, the large quantity of serosity which infiltrates it.

If, as I have already proved, the indispensable condition for the formation of the inflammatory crust, is a certain excess of fibrine in proportion to the globules, we can understand why this should not exist in the pyrexiæ, since, in these diseases, supposing them always without phlegmasial complication, two cases only can occur, one in which the fibrine has retained its normal proportion, and the other in which it has diminished.

Since the diminution of the fibrine does not exist necessarily in any pyrexia, it is perfectly clear that it is not in this alteration of the blood, that we should place the point of departure of this class of diseases. But what seems to me incontestable,

is, that the specific cause which gives them birth, acts upon the blood in such a way, that it tends to destroy its spontaneously coagulable matter, while the cause which produces the phlegmasiæ, tends on the contrary to create in that fluid a fresh proportion of that matter. If this cause act with slight energy, or if the economy resist it, the destruction of the fibrine is not accomplished; if on the contrary the cause continue to act with all its intensity, and the forces of the organism be in fault, the destruction of the fibrine will commence either at the very beginning of the disease, which is very rare, or a certain period after its commencement: all this applies itself equally well both to typhoid fever, and to the eruptive fevers. For me there is, in all these cases, a true intoxication; if it be slight, its effect must to be sure always exist, but it is not appreciable; if the intoxication be stronger, the effect which it has produced upon the blood becomes visible, and is marked in that fluid, by a diminution of the fibrine.

Whilst then we establish, in certain forms of typhoid fever or scarlatina, that alteration of the blood which consists in a tendency to the destruction of its spontaneously coagulable matter, we no more attain by this means the true cause of the disease, than we do, by studying the alterations of which the tegumentary membranes are the seat. But, as these alterations of the mucous membrane or of the skin, once produced, bear their part in the production of the symptoms, just so does the peculiar alteration of the blood, which may then arise, bear its part.

Amongst the phenomena which seem to me to have a direct connection with the diminution of the fibrine, I believe I ought to place in the first rank the hemorrhages that are so common in all the pyrexiæ in which the adynamic or putrid type predominates, that is to say those in which it has been proved by analysis that the blood had lost some of its fibrine. In variola, when the pustules are filled with blood, in scarlatina, when there are abundant losses of blood from all parts, in individuals attacked with acute purpura hemorrhagica, as well as in typhoid fevers accompanied with epistaxis and buccal hemor-

rhages which increase with the debility, I have shown that the blood was effectively very poor in fibrine, and I shall essay to prove further on that we cannot in such cases accuse the hemorrhage of having diminished the fibrine. It would seem that in this condition a certain diminution of the spontaneously coagulable matter of the blood has for effect to permit the globules to abandon more readily the vessels which contain them.

How again fail to remark the coincidence, so frequent in the pyrexiæ, of the diminution of the fibrine of the blood, and of the facility of production of those congestions or sanguine states which have so often been confounded with true inflammations? wherefore this coincidence? Deprived of the ordinary quantity of fibrine borne along with them in the torrent of the circulation, are the globules at the same time deprived of a means of regularization for their movements, and do they come in this way to accumulate and stagnate in the capillary rete? I know not; but it must be that there is some connection of cause and effect between the diminution of the fibrine of the blood and the production of these congestions, since these latter follow so constantly the former.*

There is a peculiar congestion which rarely presents itself except when there exists a typhoid condition, whatever be in other respects the disease in the course of which this condition may have arisen. This congestion has its seat in the spleen, which becomes remarkable at the same time by its great size, and by the extreme diminution of consistence of the material which fills its cellules. The softening of the spleen, noted in these cases by all observers, does not depend on an alteration of its own tissue: for it is found quite untouched, when, by washing, it has been emptied of all the material that it contains; it is evidently this latter which has lost its usual con-

* I am happy to say that all the facts, that I have just reviewed in this article, are in perfect harmony with the principles emitted, since 1837, by M. Magendie on this subject. While employing different experimental methods, we have each arrived at similar results.

sistence. But, what is this material? it is nothing more than blood retained and coagulated, I know not by what influence, in the innumerable cellules or areolæ of which the splenic tissue is composed; but this blood ought to possess the same qualities as any other blood poor in fibrine, that is to say it ought to coagulate imperfectly; whence will result, in the spleen as elsewhere, a marked softness and at the same time a large amount of clot. It is always the same cause which produces a similar kind of modification, whether in the blood that we extract from the veins during life, in that we collect from the heart and vessels after death, and in that again contained in the splenic cellules. Thus then, the augmentation in size of the spleen and its softening, which certainly accompany every well marked typhoid condition, may be regarded as the effect of a diminution of the fibrine of the blood, and this change is one of its manifestations. Let no one say moreover that it is in consequence of the greater rapidity imparted to the circulation that the spleen comes to present the changes that I have just described: for, in the acute phlegmasiæ with fever, it presents nothing of the kind.

I have already said that, however poor the blood might have become in globules, this did not prevent the temperature proper to the human body from persisting in its normal condition, and even elevating itself if there were occasion. The same is true in cases where the blood has lost a great portion of its fibrine: not only does not the temperature of the body fall in consequence, but it may even augment several degrees, just as in any other circumstance. Thus I have found it at 40° c. in cases of typhoid fever when the blood did not offer more than $\frac{1}{1000}$ in fibrine. Yet this is likewise the most ordinary temperature that we find in individuals who have fever symptomatic of an acute phlegmasia, even when the fibrine has doubled or tripled in quantity. Consequently the greater or less elevation of the temperature of the body in diseases, is not dependent upon the quantity of fibrine that the blood may contain. This temperature attains its maximum (42° c.) in intermittent fevers in which, as I have assured myself, the

fibrine of the blood remains in normal quantity;* and the average even shows itself somewhat more elevated in typhoid fever or in scarlatina than in the acute phlegmasiæ.

ARTICLE IV.

Of the Blood in the Phlegmasiæ.

I HAVE NOW shown that there is a large class of febrile diseases in which the fibrine is never increased, but is often normal, and often diminished. There are others, again, in which there is constantly an increase of this principle, diseases which are symptomatic of that sort of alteration of the solids, which from time immemorial has been called inflammation. This is not the place to criticise the vagueness and insufficiency of such an expression; but it is my duty here to set forth prominently that remarkable coincidence, in certain diseases, between the increased quantity of the spontaneously coagulable matter of the blood, and the development of various lesions of the solids, which although differing in many respects, yet resemble one another so strongly in others, that in all ages they have been classed together by nosologists, as forming a single group of diseases. And yet it must be admitted that the organic changes are much more uniform in the blood, than in the solids; amidst the diverse lesions of the latter, the blood exhibits, by the identity of the alterations which it undergoes, a disease uniformly of the same nature. Not long since, Meckel defined inflammation to be, *congestion with a tendency to new production.* The study of the blood shows the justness of this definition. For what else than a new production is this excess of fibrine which suddenly appears in the blood of a person attacked with pneumonia or erysipelas, with an inflammation of the tonsils, of the tongue, of the bronchia, or of the peritoneum? A new and redundant production of

* See in our first memoir, the results which a certain number of analyses of the blood in intermittent fevers, have given to M. Gavarret and myself.

fibrine in the blood is, then, the least variable sign of a certain number of diseases which present further analogies in the nature of the general symptoms accompanying them, and in the uniformity of the treatment they require. In my preceding essays, moreover, I have shown, that in these diseases, the other organic constituents of the blood, and particularly the globules, do not increase with the fibrine.

In the phlegmasiæ, then, there is an excess of fibrine relatively to the globules, that is to say the reverse of what takes place in typhus. Hence may be explained the physical properties of the blood drawn from a vein, in these diseases. While in the pyrexiæ, generally, the clot is bulky, flabby, and imperfectly separated from the serum, here, on the contrary it is smaller, more dense, and of superior consistence; besides which, if the blood has been properly drawn, the clot will be covered with a buffy coat of variable thickness.

I have already explained myself in regard to the value of the indications to be derived from the buffy coat. Except when it occurs in cases of anæmia, this production uniformly denotes a state of inflammation. I can cite in support of this assertion a summary of nearly eighteen hundred bleedings, in which the blood, examined by myself, never presented a buffy coat except in one or the other of two series of cases, those of anæmic patients on the one hand, and those of persons attacked with various acute or subacute phlegmasiæ, on the other. In the former, the buffy coat, which, indeed, is of moderate thickness, results from the great diminution of the globules, for the fibrine although in its usual quantity, is nevertheless in excess, relatively to the globules. But in the phlegmasiæ the globules are neither increased nor diminished, while the fibrine having become redundant, the law which governs the formation of the buffy coat reaches its full development. Moreover, the fibrine of the new product entering into the composition of the buffy coat coagulates more slowly than the old, which is another cause favourable to the appearance of the buffy coat, since the gradual coagulation of the fibrine allows the globules to sink to the bottom of the vessel, leaving the fibrine above

them, still dissolved, or suspended, in the serum. Besides, if an analysis be made for the purpose of determining the quantity of fibrine in the buffy coat, or underneath it, some indeed will be found in the latter situation, but very little compared with what can be extracted from the buffy coat itself.*

There is a striking contrast between the usually great firmness of the buffy coat, and the extreme softness of that portion of the clot which retains its colour; this softness is always great in proportion to the density of the buffy coat, and the brownish red mass which the latter surmounts, bears the greatest resemblance to imperfect and half liquid currant-jelly. On examining this mass through a microscope, an accumulation of globules is found in it, while none, or very few, can be

* With reference to this subject I have studied the clot in three cases of pneumonia, and in two of acute articular rheumatism. In these five cases the fibrine of the clot was apportioned in the following manner:

First case of pneumonia.	
Fibrine of buffy coat - - - - -	8.1
Fibrine of rest of clot - - - - - -	1.1
Total fibrine	9.2
Second case of pneumonia.	
Fibrine of buffy coat - - - - -	5.8
Fibrine of rest of clot - - - - - -	3.2
Total fibrine	9.0
Third case of pneumonia.	
Fibrine of buffy coat - - - - -	4.8
Fibrine of rest of clot - - - - - -	2.5
Total fibrine	7.3
First case of articular rheumatism.	
Fibrine of buffy coat - - - - -	7.0
Fibrine of rest of clot - - - - - -	1.6
Total fibrine	8.6
Second case of articular rheumatism.	
Fibrine of buffy coat - - - - -	7.5
Fibrine of rest of clot - - - - - -	1.7
Total fibrine	9.2

detected in that portion of the clot which forms the buffy coat.

On examining the latter in the earliest periods of its separation, and before the coagulation is visible to the naked eye, or just as it is commencing, certain phenomena may be witnessed; such I have verified with M. Gavarret, and which I will now describe..

We received in a glass vessel 80 grammes (about 2½ ounces) of the blood of a person suffering from acute pneumonia; the coagulation took place as usual, and a buffy coat soon made its appearance upon the surface of the clot. Hardly had the yellowish and opaline liquid which constitutes its first rudiments appeared above the mass of globules, when we placed a drop of it under the microscope; then, in addition to some red globules, the field of the instrument appeared to us filled with those grain-like corpuscles whose nature I have already endeavoured to determine. The opaline liquid became every moment more consistent; when it assumed the appearance of a tremulous jelly denoting its approaching solidification, we again examined it under the microscope, and saw forming before our eyes numerous very fine fibres, resembling long and very delicate threads, crossing one another in various directions, so as to leave intervals between them of variable extent, and giving to the whole the appearance of a net-work. These fibres, at first, few in number, and scarcely visible, became more numerous and more distinct, until they occupied the whole field of vision; and, as they increased, formed superposed planes at certain points, where the net-work was succeeded by an appearance like felt. The fundamental form, however, continued to be reticular. As the solidification of the buffy coat proceeded, this appearance of interwoven fibres disappeared, and there only remained visible a confused and amorphous mass.

I have repeated this experiment several times, and always with the same result. I have also examined with a microscope the sero-fibrinous liquid which may be separated from the globules, as already stated, by subjecting the blood to the

action of sulphate of soda, and then, upon examining the flakes which quickly appear in the liquid, I have found these same reticulated fibres. I shall avail myself hereafter of this microscopical sign afforded by the fibrine of the blood, to prove the identity of this principle with other spontaneously coagulable matters, which, in certain cases, are found mixed with the serosity.

Here, then, is the necessary, the indisputable modification offered by the blood in every inflammation acute enough to be accompanied with fever, the creation in that fluid of a new quantity of fibrine. Here we have an explanation of the physical properties of the blood in the phlegmasiæ, so different from what they are in the pyrexiæ: here too the cause of the formation of the buffy coat, whose fibrinous nature is thus demonstrated as well by microscopical examination, as by chemical analysis.

This spontaneous production of an excess of fibrine in the blood is, moreover, independent of the various conditions in which the system of the individual attacked with inflammation may happen to be. For, remarkably enough, it does not fail to take place even when a phlegmasia occurs during the course of typhoid fever, the influence of which is to create, at least, a tendency to lessen the quantity of fibrine in the blood. The real increase of the fibrine in such a case is not, however, very great, for I have never found its maximum to exceed 5½, which number corresponds to one of the lowest degrees of the inflammatory state, and in other cases the amount of fibrine was even less, its increment was only relative. Does it not, then, seem as if the fibrine were controlled by two forces, one of which, represented by the intercurrent phlegmasia, urges its increase, and the other represented by the typhoid fever, acts in the opposite direction, and reduces to its minimum the influence of the phlegmasia? In this way we may understand how the fibrine, although exceeding its physiological quantity in cases of typhoid fever complicated by intercurrent inflammation, is yet developed in a less degree than if its

increase were regulated only by the laws of the inflammatory state.

Although the constitution may be exhausted by a chronic disease, or a more or less complete state of anæmia be established, the fibrine will nevertheless be augmented under the influence of whatever inflammation may supervene. Nor is there any thing surprising in this; for, in the supposed circumstances, the globules diminish, while the fibrine remains normal, so that its increase, through the intervention of the inflammatory state, is less singular than in the case of typhoid fever. In the above mentioned conditions of the economy I have seen it increase much more than in typhoid fever. In chlorotic patients, for instance, who had been attacked with acute articular rheumatism, capillary bronchitis, pneumonia, or erysipelas, I have found the blood to contain 6, 7, and even 8 parts of fibrine. While, therefore, clinical observation demonstrates the frequent coincidence of anæmia and inflammation, chemical analysis discloses to us in the composition of the blood, circumstances which far from opposing this coincidence, should rather be held capable of favouring its development. For since in all cases of general debility the globules are diminished, and the fibrine relatively increased, it follows that in the spontaneous anæmia occurring towards the close of many chronic diseases, the proportions of the several constituents of the blood to one another are such that the state of this fluid approximates more nearly to the change of composition effected by inflammation, than under any other circumstances, so that the blood may be said to have then a sort of predisposition to the inflammatory state.

I have not observed that, apart from the disease itself, the differences of constitution or temperament, of age or sex, modified in any notable degree the quantity of fibrine in the blood. Whether the individuals attacked with acute inflammation were strong or feeble, of a sanguine or lymphatic temperament, the increase of the fibrine was neither more nor less considerable, following only, amidst these various conditions of the organism, the variable intensity of the inflammation.

I was much struck by a fact observed in some experiments which I undertook with M. Gavarret in order to settle the composition of the blood in animals deprived of food. This fact was a remarkable increase of fibrine; but my surprise was at an end when, upon the dissection of these animals, I discovered in their stomachs lesions of the most clearly inflammatory nature, such as bright redness, softening, and numerous ulcerations of the mucous membrane. From that time, I have seen in those experiments only a confirmation of the principle I have just now laid down, to wit, the possibility of an inflammation developing itself in spite of the general debility of the system, and the simultaneous increase of the fibrine of the blood in spite of the general impoverishment of that liquid. The following are some details of those experiments.

We bled three healthy and well kept dogs. Their blood contained fibrine represented by 2.3; 2.2; and 1.6 respectively. These variations are ordinary and physiological in canine blood, as I have elsewhere shown.* After having thus determined the composition of their blood, these three animals were made to fast, more or less rigorously, until they died.

From the first both food and drink were withheld from December 21st 1841 to January 11th 1842, when he died. During this period he was twice bled, on December 28th and January 4th. The quantity of fibrine in his blood rose from 2.3 to 3.9 and 4.5.

The second dog was not allowed to eat from December 21st to January 8th, the day of his death; but all this time he was permitted to drink water. He was bled December 28th, January 4th and 8th, and the fibrine of his blood had risen from 2.2 to 2.9 and 4.0.

The third dog was not starved so absolutely: from December 21st to January 16th he received every morning a small ration of soup. He was first bled December 28th, and again January 4th, but there was no considerable increase of fibrine, although it was far from diminished, being represented by 1.8

* Mem. cit.

instead of 1.6. Such was not the case, however, on January 12th, four days before the animal's death, and when the influence of insufficient food had been longer felt by the organism. In this third bleeding the increase of fibrine was very marked; it had reached 3.3. The proportion was indeed less than in the other cases; but it is worthy of remark that this third dog had not been entirely deprived of food, and was the only one whose stomach was not ulcerated; the redness of his gastric mucous membrane was also less general and less vivid.

Need I here recall the fact, that independently of the interest which belongs to these experiments in relation to the subject in hand, they entirely confirm the opinions which, ever since the time of Hunter, have prevailed in our science respecting the morbid and excessive excitement, and the inflammatory disorganization, which may affect the stomach when, for a certain period, it has either received too little food, or none at all?

No matter, then, what may be the state of the system, the supervention of an acute phlegmasia involves necessarily, and in every case, the increase of the fibrine of the blood beyond its normal quantity. This law, too, prevails amongst animals, as well as amongst men, as I have become well assured by analyzing the blood of dogs, horses, neat-cattle, and sheep, attacked with various inflammations which had been discovered during life, and after death.

In man, when an acute inflammation is well established, the fibrine varies in quantity between 6 and 8; in a smaller number of cases it rises as high as between 8 and 9; and, more rarely still, exceeds the latter number, and reaches by degrees $10\frac{1}{2}$, which is the highest number I have yet found representing the fibrine in phlegmasiæ attacking the human race, though in a neat affected with pneumonia I found it as high as 13. It must be remarked here, that since the physiological number representing the fibrine in animals is not the same as that for man, the increment in the former must not be judged of by the standards of the latter, but must be referred to the average obtained for each particular class of animals. Thus the physiological mean of the fibrine in dog's blood being only 2.1,

the numbers 3, 4, and 5 obtained when this animal was attacked with inflammation, would, in the case of man, indicate a development of fibrine to be represented by much higher numbers. On the other hand, the physiological mean of the fibrine in the blood of horses and neat-cattle being greater than that of man, the number 13 indicating the quantity of fibrine in the blood of one of these animals, would, in the case of man, represent a much inferior quantity. These corrections are indispensable, if we desire profitably to apply to human pathology the results obtained from studying the pathology of other species.

In regard to the cases in which the fibrine falls below 5, they are either acute and slight inflammations, and which can hardly be said to have commenced, or whose activity and extent are inconsiderable: in them it may happen that the fibrine falls from 5 to $4\frac{1}{2}$, and sometimes even to 4; but this last number represents the lowest possible, and, as it were, exceptional limit, of the quantity of fibrine in the acute or subacute inflammatory state.

To demonstrate the sudden change of composition which takes place in the blood of persons attacked with acute phlegmasiæ, I might cite several cases in which the same person having been bled, some days before the outset of the phlegmasia, and again during the course thereof, his blood, which contained the normal quantity of fibrine at the first depletion, was much more abundantly provided with it at the subsequent ones.

The two diseases in which I have noticed the greatest development of fibrine, are pneumonia, and acute articular rheumatism; they are the only ones in which this augmentation reached the number 10.

I will now pass in review all those diseases, different indeed in seat, but not in nature, in which I have found, as an invariable characteristic, an increase in the spontaneously coagulable matter of the blood.*

* For further details respecting the state of the blood in these various diseases, see the two memoirs already cited, and which are published in the

And first, since inflammation of the cellular tissue is regarded as the type of all inflammation, I will notice a case of phlegmon of the leg, of moderate extent, which terminated in abscess, and which was accompanied by a very slight febrile reaction. The first bleeding gave 4.7 of fibrine, the second 5.

In another case of phlegmon of the breast which terminated in resolution, the blood furnished 4.5 of fibrine during the course of the affection, and only 3.7 at its close.

Out of 84 bleedings performed in the course of well marked cases of pneumonia, there were seven only in which the fibrine varied in quantity between 4 and 5; in the 77 others it exceeded the latter number, was eleven times between 5 and 6, nineteen times between 6 and 7, fifteen times between 7 and 8, seventeen times between 8 and 9, nine times between 9 and 10, and six times at, or a little above, 10.

In inflammations of the mucous membrane, the quantity of fibrine is found to remain normal, if the inflammations are slight, limited, and without fever; but do they acquire ever so little of a certain degree of intensity, and manifest a febrile reaction, so surely does the fibrine of the blood augment.

Thus I have seen it reach 6, 7, and 9 in cases of bronchitis of great extent and acuteness. I refer to my first memoir for the details of these cases, contrasted with others of chronic bronchitis in which there was no increase of the fibrine. Inflammations of the intestinal mucous membrane present the same phenomena.

I may here be permitted to cite, somewhat less briefly, four cases of acute mercurial stomatitis which seem to me to possess some interest due, on the one hand, to the cause producing them, and, on the other, to the exact ratio which existed, in all these cases, between the intensity of the affection of the solid, and the quantity of fibrine in the blood. These four cases have, moreover, never been published.

In the first a slight stomatitis occurred after a dose of twelve

Annales de chimie et de physique, vol. lxxv of the 2d series, and vol. v of the 3d. I shall here only notice at any length the facts not published in these two memoirs.

decigrammes (18.5 grains) of calomel; there were a few pseudo-membranous films scattered over the lining membrane of the mouth; the salivation was copious; the pulse 80; the temperature of the skin 37.50.* The blood contained 4.5 of fibrine.

In the second case a dose of only six decigrammes (9.5 grains) of calomel had given rise to a rather more acute inflammation of the mouth; and there was more fever. Pulse 100; temperature 39. The blood contained 5 parts of fibrine.

In the third case, the affection followed the use of mercurial frictions simultaneously with calomel given internally; it was more violent than the two preceding cases. Numerous and thick false membranes invested the gums, the lips, and the cheeks. The degree of fever was about the same as in the second case, (pulse 96, temperature 38.50,) we found 8.4 of fibrine in the blood.

In the fourth and last case, the stomatitis, produced as in the last case, was more considerable, for the whole mouth was enormously swollen, and encrusted with false membranes. The pulse was 120, the temperature 39. In this case the fibrine rose to 6.6, and its increase was clearly due to the inflammation; for the patient had, a few days before, been bled for a slight cerebral hæmorrhage, and at that time his blood contained only 3.5 of fibrine. In the other three cases, there was no other affection before the mercurial sore-mouth, which could have produced any modification in the amount of fibrine in the blood.

Mercurial stomatitis, therefore, notwithstanding its specific nature, does not differ from ordinary inflammations in its influence on the blood; and yet it has been asserted again and again, that one of the effects of mercury introduced into the system is to bring about a state of dissolution of the blood, which is incompatible with an increase of fibrine. It is possible that this may take place after a prolonged use of the medicine, but assuredly such is not the case soon after its first

* Probably centigrade: but the author does not mention what thermometer was used by him. *Tr.*

exhibition. Consequently, when it is administered to combat certain acute phlegmasiæ, such as peritonitis, it is not right to assume that its antiphlogistic action consists in its producing in the blood a condition opposed to that which belongs to the inflammatory state. Nor do I find that this dissolving influence upon the blood which is claimed for mercury, has ever been demonstrated, in any alleged case, by a rigorous examination of that fluid. It appears to me that the opinion rests chiefly on a fancied analogy between the effects of mercury, and those of scurvy, upon the mouth.

But this is a deceptive resemblance: in the affection of the mouth following the administration of mercury, are to be observed all the marks of a true inflammation, which, if somewhat intense, is accompanied with active fever. But the case is not the same in scurvy: the symptoms which then show themselves in the mucous membrane of the mouth are only amongst the phases of those hæmorrhagic congestions which are ready to take place in nearly all the tissues.

Proceeding with the exposition of our analyses of the blood in various cases of inflamed intestinal mucous membrane, I find it to be uniformly the fact, that a notable increase of the fibrine takes place whenever any portion of this membrane, from the fauces to the end of the colon, inclusive, is attacked with inflammation acute enough to excite fever: in these cases the quantity of fibrine has reached 5, 6, and 7, but never a higher degree. We have already shown that this increase does not occur, when the inflammation, seated in the follicles, exists only as one of the elements of a general disease, i. e. of a typhoid fever.

The great distinctive traits separating cholera from proper inflammatory affections of the intestinal canal, might have found confirmation, if need were, in a recent examination I had occasion to make of the blood, in a perfectly sporadic case of this disease. The patient was a robust man, in middle life, who entered the hospital of La Charité with all the symptoms of a pretty severe attack of cholera: (copious vomiting and purging, colourless stools resembling rice water, cramps, apho-

nia, suppression of urine, cold skin, but a pulse of natural fulness, and moderate frequency.) The blood of this patient gave only 3.3 of fibrine, and contained only 118 parts of globules, and 88 of the solid constituents of the serum.

Finally, to close this review of the state of the blood in inflammations of the mucous membranes, let me remark, that the increase of the fibrine has not failed to occur, either in various cases of acute cystitis, whether accompanied or not with nephritis, or in recent, painful, and intense inflammations of the utero-vaginal mucous membrane. In these different cases, which were all accompanied with fever, the fibrine oscillated between 4, 5, and 7. I may mention that one of these cases was complicated with Bright's disease of an indolent and apyrectic form, to combat which I directed a bleeding which gave 3.6 of fibrine. Three or four days afterwards an acute pain attacked the right side of the lumbar region, and fever set in. The patient was again bled, and this time his blood, suddenly changed in its composition, contained 5 of fibrine.

Inflammations of the skin, as well as of the mucous membranes, bring with them an increase of the fibrine of the blood. This I have ascertained in a person who had been severely burned; while, on the other hand, there was no increase in another whose burn was slighter, and less extensive.

It appears to me peculiarly interesting to determine, whether, in cases of burn, the blood becomes charged with fibrine, because in such cases, evidently, the disease begins in a solid, and the alteration of the blood can therefore only be regarded as consecutive. Further on I shall revert to this subject.

The course of erysipelas, when acute and febrile, is like that of a burn, and shows an increase of fibrine represented by the numbers 6 and 7. The pustules of variola, and the exanthema of measles and scarlatina, like the follicular affection in dothinenteritis, exert less influence upon the blood, than simple erysipelas.

I have likewise established this invariable law of augmen-

I have likewise established this invariable law, of augmentation in the fibrine of the blood, in regard to every acute inflammation of the serous membranes. It was, for instance, very marked in a case of cerebro-spinal meningitis, in which, after death, I found the spinal marrow surrounded, in its whole extent, by a sort of purulent sheath, the pus having infiltrated the pia mater.

In pleurisy, peritonitis, and pericarditis, I have also found in the blood this same excess of spontaneously coagulable matter. These various cases, 24 in number, are divisible into two series. The first comprises those in which the disease, whether acute or chronic, was accompanied with fever, and continually grew worse; which suggests the probability that the primary cause of the disease was not exhausted, but maintained its action. In the cases belonging to this series, I uniformly found an excess of fibrine in the blood, its minimum being 4, its maximum 8.4.

In the second series, other facts present themselves. The inflammation seemed to be suspended; the pulse lost its frequency; and the only remains of the disease were a greater or less effusion into a serous cavity. The blood then ceased to contain an excess of fibrine. It may even happen, as I once saw, that this principle, although excessive at the commencement of the disease, may return to its normal proportion, while yet the fever persists, but only after the prolonged duration of the malady has caused extreme emaciation.

The case referred to is that of a woman attacked with peritonitis; during the earlier stages I had her bled twice; the blood gave 5.3 and 5.4 of fibrine. The peritonitis lost its intensity after this depletion, but was not cured, and gradually passed into a chronic state. The patient was already much emaciated, when I endeavoured, by another bleeding, to diminish the fever, which had never for a moment ceased. This time the blood contained only 3.5 of fibrine. After this bleeding, there was no improvement, and the patient sunk speedily. The intestinal convolutions were united by organized false membranes, and the pelvis was filled with pus. The tempe-

rature of the skin, even to the last day, remained at 40° cent., and the blood did not then contain more than 68 parts of globules.

In addition to these 24 cases of serous inflammations, I should cite another, in which the fibrine was so small in quantity as to contrast with all the other acute and recent cases. The form of the disease was, moreover, quite peculiar. It was seated in the pleura; indeed commenced like a simple pleurodynia; and then without any initial chill, or frequency of pulse, a considerable effusion took place rapidly on one side of the chest. In this singular case of pleuritic effusion without fever, the fibrine in the blood preserved its normal quantity, (3.5). It may be doubted whether there was, in this instance, a real inflammatory process. Was it not simply hydrothorax?*

There is a disease which, in many respects, seems to differ from ordinary inflammations, but which, like them, obeys the law relative to the fibrine of the blood. I allude to articular rheumatism. If acute, the fibrine augments uniformly, as has been proved to me by an analysis of 43 bleedings, in which the fibrine was once represented by 4, six times by 5, fifteen times by 6, thirteen times by 7, three times by 8, three times by 9, and twice by 10.

But if the articular rheumatism be only subacute, there is less fibrine, although it generally exceeds the physiological quantity. In six cases of the sort it varied between 4 and 5.

If, finally, the articular rheumatism be decidedly chronic, the fibrine returns to its normal standard.

To bring this long catalogue to an end, I have yet to point out the modifications of the fibrine in certain inflammations of the parenchymatous tissues, regretting, at the same time, that I am unable to furnish more cases in point. But, thus far, I have not had the opportunity of collecting them.

In two cases of acute inflammation of the lymphatic ganglia of the neck, with fever, I have seen the fibrine reach 4.2

* The details of this case may be found in my first memoir upon the alterations of the blood, p. 74.

and 5; one of these cases is the more conclusive, because the blood of the patient, who was bled for another reason, two days before the attack of ganglionitis, gave only 2 parts of fibrine.

In a case, proved by the autopsy to be acute nephritis, this element reached the number 7.

In conclusion, I give another illustration of the state of the fibrine in a case of softening of the brain. A woman was brought to the hospital labouring under a recent attack of apoplexy. Her limbs were paralyzed and rigidly flexed. I had her bled, and was struck with finding a larger quantity of fibrine in her blood (4.5) than is usually found in simple hemorrhages. She soon died, and the autopsy disclosed, in the right corpus striatum, and around a clot, a red softening of the cerebral substance, of small extent, but very distinct. Inflammation had, then, existed around the apoplectic centre; the contraction of the paralyzed extremities had indicated it during life, and the excess of fibrine in the blood had added to the value of that sign. It should also be remarked here, that if the excess of fibrine was small, the inflammatory complication was also very limited.

Since the commencement of my inquiries, I have not met with a single case of acute hepatitis, a disease known to be rare in our climate. I have several times analyzed the blood of persons affected with jaundice, but found no increase of fibrine in any of them; nor yet in a simple case of hepatic cirrhosis.

The increase of fibrine in the blood takes place from the very commencement of the inflammatory state. I have frequently had the same individual bled twice; the first time, on the day previous to the inflammatory attack, and the second time, a few hours after its distinctly marked invasion. The first time, the fibrine of the blood was normal, the second, in excess. I have, thus far, vainly striven to determine whether or not the composition of the blood was modified, before the change denoting inflammation appeared in the solids; I have not succeeded, and my analyses have proved to me nothing more than the simultaneous origin of these two phenomena. This serious question does not yet, however, appear to me to

be set at rest; a question, by the ultimate solution of which we must decide, whether in the great phenomena of inflammation, the source of disease is in the solids, or in the blood, or whether the alteration of the one is not so essential to that of the other, as that both must necessarily begin to exist at the same moment. Remark, too, what a variety of beginnings belong to the diseases ranked as inflammations: at one time there is no interval between a state of perfect health, and the invasion of the disease; at another, there is a general uneasiness, and that slight disturbance of all the functions which we call the "prodrome" of diseases; at another, a well marked fever sets in, from one to three days before the appearance of symptoms denoting a phlegmasia of some one of the solids. But even where the disease comes on without any "prodrome," it may do so in one of three ways: either there is pain, a purely local symptom, to open the attack, while the rest of the economy seems unaffected by the local disorder; or before this latter is felt, there may be a violent chill as the only appreciable morbid phenomenon, and which may last for half an hour, for an hour, or even longer; or else the local symptom and the chill may appear simultaneously. I ought to add that this last case is more common than the two others. We may well inquire whether, when its earliest symptoms are so different, the starting point of inflammation is always the same. That which takes place in the case of a burn proves very clearlyt hat, under the circumstances, the blood is modified in its composition subsequently to the alteration of the solid, and, inferentially, we may suppose that it must be so in all other inflammations. The analyses of the blood hitherto made would tend to confirm this view, for they have never revealed an excess of fibrine in the blood, before the occurrence of inflammatory symptoms in the solids. On the other hand, there are certainly cases in which the sensible alterations of the latter are so inconsiderable, so variable, and sometimes so ephemeral, that it is difficult to understand how they can be the cause of such intimate and enduring changes as have then taken place in the blood. Is it not often so in articular rheu-

matism, and is it not remarkable that this is one of the diseases remarkable for increase of fibrine? In all this there are unknown quantities to determine: there is yet to be discovered that mysterious link, whose necessity is proved by its constancy, and which, in the phlegmasiæ, unites the alteration of the solids with that of the blood. Yet, from the simultaneous character of these alterations, the deduction may still be made, that what we call inflammation is not a disease seated in the solids merely, that it does not influence the rest of the economy only by pretended sympathetic radiations, and, that in all these things, the changes which are then taking place in the blood, play an important part. An inflammation, then, is not a purely local disease. Does the fever which accompanies every acute phlegmasia of some intensity depend upon the excess of fibrine contained in the blood?* Observe that there is still an almost constant and reciprocal relation to be studied, between these two facts; for, as the fever begins, the fibrine increases, and as the fever ceases, the fibrine returns to its normal condition, yet the local lesion may still persist with considerable activity. How many times, for instance, have I not continued to find, by auscultation, the most perfectly distinct signs of pulmonary hepatization, when, for several days before, all fever, and every appearance of reaction between the lung and the system, had completely disappeared; so completely, that but for auscultation, one might have believed the disease at an end. And indeed it was so, in this sense, that the lesion of the lung was only the result, and almost an unimportant one, of a morbid action that had ceased; thenceforth the fever also ceased, and the production of new fibrine, the index of this process in the blood, no longer took place. The disease had once more become entirely local, if indeed such a condition of the lung deserves the name of disease. It would be said, in the language of some of the schools, that the diathesis no longer

* At any rate we should be able to explain only the symptomatic fever of acute phlegmasiæ, in this way; for in the pyrexiæ the fever is long, and intense, without there being an excess of fibrine in the blood.

existed. But what is meant by this expression? To point out the existence of a general condition of the system of the same nature as the local lesion, and which causes the whole organism to share the suffering of one of its parts. There is not, says Tommasini, an inflammation, properly so called, without the production of a diathesis; a local irritation caused by a thorn run into the finger, does not, according to this author, become an inflammation, unless, in consequence of this very circumscribed lesion, the sthenic diathesis should be established; and it is established, he adds, by the diffusion of the phlogosis of the vessels around the injured point, to those of the rest of the body. This theory is nothing more than the emphatic announcement of the important fact that the whole organism participates in the morbid operations which seem confined to a single one of its points. Who does not see, that in other words, and in another aspect, it is this same fact upon which is founded the law requiring the production of new fibrine in the blood, as soon as any solid becomes the seat of an inflammation intense enough to give rise to more than what Tommasini calls a simple irritation? Is not the excess of fibrine then produced, the material representative, as it were, of what Tommasini terms the diffusion of phlogosis? Thus it is that we reach the same conclusion, in spite of the suggestions of different theories, and of opposite methods of observation.

The formation, then, of an excess of fibrine in the blood is uniformly the accompaniment of inflammations of a grade high enough to give rise to fever; but this fact acquires a greater importance both as a diagnostic sign, and as an element of the doctrine which relates to the production of disease, if we reflect that it never takes place unless an inflammation exists somewhere. An excess of fibrine in the blood becomes, therefore, a pathognomonic sign of such inflammation.

There is, however, a circumstance, occurring even during health both in man and the lower animals, which has the power of augmenting the proportion of fibrine contained in the blood; I allude to gestation. But this augmentation, which is

found only at certain epochs of pregnancy, is rather a high physiological maximum, than even the ordinary degree of pathological increase. The following are the results obtained by M. Gavarret and myself from analyzing the blood of 34 pregnant woman.

From the first to the end of the sixth month, the blood contained less than its average physiological proportion of fibrine; the mean of the fibrine during the first six months being only 2.5; its minimum 1.9; and its maximum only 2.9.

On the other hand, during the last three months of pregnancy, the mean of the fibrine exceeded the physiological mean; it reached 4, and the maximum rose to 4.8.

And, further, it was found that the increase of the fibrine had become greatest in the last month of pregnancy; at this period its mean was 4.3; its maximum was not reached until the access of labour, and it may be presumed that this maximum was maintained, if not exceeded, for some time after delivery. It seems to me that this presumption is supported by the results which I obtained with MM. Gavarret and Delafond, by analyzing the blood of sheep and cows during their gestation, and again after they had brought forth; at which latter time these animals furnished more fibrine than before. (See the Memoir upon the composition of the blood in certain domestic animals.)

It is then demonstrated that in women, at particular periods of gestation, and in cows and sheep, after parturition, the blood contains a certain excess of fibrine. The blood, on these occasions, shows a remarkable tendency to assume the character of inflammatory blood; and, assuredly there is matter for reflection in the relation which may exist between the modification then effected in the blood, and the development of those peculiar attacks, generally of an inflammatory aspect, to which women in childbed are so liable. But ought the slight excess of fibrine in their blood, at that time, to be regarded as a predisposing cause of these attacks? If so, this would be such a case as I recently sought, (and observation has not yet furnished me with any other) in which the proper inflamma-

tory alteration of the blood precedes the signs of inflammation in the solids.

If in the later periods of pregnancy the blood contains rather more fibrine than in other states of health, we may understand how it happens, that when blood is drawn from a certain proportion of pregnant women, its clot should be covered with a buffy coat; and this should occur the more readily in them, because the amount of globules in their blood often falls more or less below the normal standard. Thus, of 34 pregnant women whose blood we examined, in one only who had reached the end of her second month, did the globules, (145) exceed the physiological average; this woman was plethoric, and the quantity of her fibrine was only 2.8. In another case of pregnancy of from one to two months, the globules reached exactly the normal average, 127. But in the 32 others, they fell below this point, varying in six cases from 125 to 120, and in the 26 other cases from 120 to 95; whence it follows that there was a commencement of anæmia in all these women. This state of the blood, is also perfectly in keeping with the remarkable pallor, and the degree of puffiness of the face, which many women exhibit, as soon as they have conceived. Pregnancy, then, which has often been looked upon as a cure for chlorosis, rather disposes some women to the affection while that state lasts.

But enough about this subject, upon which I have entered here only that I might render prominent the curious analogy that exists between the blood of pregnant women, and that of persons attacked with acute inflammations.

Before concluding our notice of the state of the blood in inflammation, I wish to direct the attention, for a few minutes, to the nature of those alterations which may occur in the solids. These products are either the natural secretion of the inflamed part, modified both in quality and quantity, or else pus, or some of the elements of the blood itself. I shall, in this place, allude only to the third form.

The two principal elements of the blood which are the most frequently separated from it, in inflammation, are albumen and

fibrine. But although the albumen of the serum may be given up by the blood in many conditions of disease which have no connection with inflammation, such is not the case with the fibrine, which does not leave the blood, in disease, except to be deposited in the tissue, or upon the surface, of organs whose texture has been altered by inflammation.

The serum contained in an inflamed solid, moreover, as well as that which is separated from the blood under any other circumstances, never exactly resembles the serum of the blood, in the proportion of albumen it contains. It may be laid down as a general principle that morbid secretions of serum, whatever be their origin, are rarely as rich in albumen, as the serum of the blood; but, other things being equal, those which most closely resemble the serum of the blood in the quantity of albumen they contain, sometimes even equalling the proportion contained in that fluid, are such as are exhaled from inflamed surfaces. I shall demonstrate this in a subsequent article upon the state of the blood in dropsies.

I have also endeavoured to discover how much albumen was contained in another variety of serum, that of a congestive abscess, and which had suspended in it a large quantity of pus-globules. To the naked eye this liquid appeared turbid, and of a milky hue; but by filtering, we easily deprived it of the globules that diminished its transparency, and then we obtained a liquid so perfectly resembling pure serum in all its physical properties, as not to be distinguishable from it. This liquid, thus deprived of the matters suspended in it, we subjected to the ordinary processes, and found that it contained a proportion of albumen nearly equal to what exists in the healthy blood; a result confirmatory of the principle just now laid down.

We learn, besides, from this experiment, that a portion of the liquid furnished by an inflamed solid is nothing more than the serum of the blood, with which is mixed a greater or less number of those singular bodies called pus-globules.

Thus, one effect of the morbid process, called inflammation, is to deprive the blood of a certain portion of its serum; the

latter, as may be conceived, is not then altered in its essential nature, but undergoes a change of aspect dependent upon the admixture with it of two new bodies; a principle (fibrine) which, like the serum itself, is an emanation of the blood, and of a matter (pus) which, as regards its physical properties, at least, has nothing like it in the blood.

This process, then, whose nature is wholly unknown, and which cannot be accomplished without the blood is overcharged with fibrine, determines, whenever it takes place, the elimination of a certain quantity of fibrine. But this elimination is not always distinct; it is especially observed, and in the most evident manner, either in the serum formed upon the skin by the action of cantharides, or in that which fills the cavities of inflamed serous membranes.

It is not only at this day that the spontaneously coagulable matter found in these liquids has been considered fibrinous; but there was no ground for its being so called, other than its property of becoming solid. To demonstrate that this substance was really fibrine, I adopted another method of investigation: I examined, under the microscope, the flakes which the serum holds suspended, and also the yet soft false membranes lining the free surface of inflamed serous membranes, and found, in both instances, a net-work precisely similar to that presented by the fibrine of the blood, and which has already been described. Thenceforth I no longer doubted that the flake-like matter which swims in the liquid produced by blisters, and the false membranes of serous tissues, were really composed of a substance perfectly analogous to the fibrine of the blood.

I have not yet had an opportunity of determining whether or not this net-work, which is so characteristic of the presence of fibrine, is to be found in the pseudo-membranous layers which, in certain cases, cover the mucous membranes. To the naked eye, these concretions are far from resembling the serous false membranes, and it may be, that under the influence of some pathological action, other principles, besides the fibrine, acquire the property of coagulability. Who knows

how far the habitual acidity of the mucous membranes, and of the skin, may favour this coagulation of the albuminous principles which are thrown upon the free surface of these organs, either accidentally, or in consequence of disease?

But what is the nature of pus, and the mode of its formation? It is very difficult to resolve these questions in the present state of science. I cannot admit, as has been maintained by some, that the globules of pus are a transformation of those of the blood; there is such a difference in their very nature, that if a little ammonia be added to a mixture of pus and blood placed in the field of a microscope, the globules of the blood are seen to disappear, while the globules of pus are in no wise changed. Nor is the pus formed at the expense of the serum, the albumen of which is found unchanged, the pus being merely suspended in, without being, the least in the world, confused with it. If a mass of pus be treated with nitric acid or alcohol, granite-like plates are seen, by the microscope, to form, just as in all serum treated in the same way, but the pus-globules undergo no change. May not, then, the pus-globules be nothing more than a modification of fibrine, which, instead of reaching the net-work form, has remained in the serum in that state of granular corpuscles, whose origin and nature I have already pointed out? May not these corpuscles, grouping themselves together with a certain regularity, produce the globules of pus? Shall I say, in favour of this view, that on examining with the microscope the sero-fibrinous liquid separated from the blood-globules by means of sulphate of soda, I happened, more than once, to see the corpuscles that were swimming in the liquid, arrange themselves in little masses which appeared to me to have the most perfect resemblance to pus-globules? It would have been quite impossible to show any difference between them. And further, in the microscopic examinations of pus, not only are voluminous and regular globules observed, but alongside of them is seen a large number of little molecules precisely like those which swim in the serum of the blood, and which evidently approach one another, unite together, and at last become ag-

gregated in rounded masses. If finally, we examine attentively a well formed globule of pus, it appears to be made up of a collection of globules placed in juxtaposition, rather than blended. It is not, certainly, a body formed in a single piece, and constituting a perfectly homogeneous whole, like the globules of the blood.

Thus two substances are revealed by the microscope, the one globular, the other reticular, which characterize the presence of the morbid process, termed inflammation, in the solids. The reticular substance is nothing more than fibrine identical with that of the blood; the globular substance is perhaps this same fibrine, but altered in its nature, and arrested in its coagulation. These two matters have, moreover, very different destinies. One of them, the reticular, is capable of assuming organization; vessels may be seen to ramify in it; it may become a tissue; this it is which forms adhesions, or which, under the name of coagulable lymph, places itself between the lips of wounds and becomes the medium of their union; far from causing injury by its presence, it is, then, in certain cases, the means of reparation to the tissues, and to that end it lives with their life, and ends by identifying itself wholly with them. But such is not the case with the globular matter. Whether or not it have a common origin with that last mentioned, certain it is, that it constitutes a product which cannot remain within the solids without affecting, more or less, the whole economy; it is incapable of organization, and reveals no trace of vitality. While the organism tends, in some sort, to assimilate to its own proper use the reticular substance, and employs it to repair the mischief it originally caused, it strives, on the contrary, to expel the globular matter, whose presence is pernicious; so long as it is not eliminated the disease persists, and this elimination itself is not always effected without serious accidents. But can the globular matter, instead of being merely expelled, and after having been conducted more or less rapidly to those surfaces in direct communication with the exterior of the body, disappear from the place where it was formed, and enter directly into the circulatory torrent?

It is not easy to understand how such large globules as those of pus can penetrate in mass, by a sort of endosmosis, through the coats of the vessels; at the most, they could traverse them only in fragments, and, as it were, in ruins. But once received into the blood could they again unite, and re-form new globules? I do not wish to exhaust this question; and indeed I do not think it can be resolved by the facts we at present possess. Still, I will say that the presence of pus-globules in the circulating fluid, appears to me, after what I have seen, a fact that can in no wise be contested. I have found, more than once, in the midst of blood-globules taken from the vessels of dead bodies, globules of pus, well formed, and so distinctly characterized that they could not possibly be taken for any thing else. They were, certainly, neither altered globules of blood either jagged or granulated, nor those white globules which are found mixed with the ordinary red ones, and which, besides, could not be confounded with globules of pus. The following cases are those in which I met with them.

The first is that of a person who was brought, dying, into the hospital of La Charité, and in a very marked ataxo-adynamic state. At the dissection I found very numerous abscesses in the brain, the lungs, the kidneys, and the spleen. The blood was everywhere either quite liquid, or grumous, and like thin currant-jelly. I collected a small quantity of blood from the crural vein for examination by the microscope; in the midst of a great many disfigured and granulated globules of blood, (for such is their ordinary condition in the dead body,) a considerable number of pus-globules could be very distinctly made out. There was nowhere the least trace of phlebitis. This is one of the cases which the older writers would have designated under the name of purulent diathesis. Collections of pus in several of the solid organs, and pus in the blood, were in reality, the only lesions that could be detected.

In another case I found pus in the blood under the following circumstances. A labourer had been wounded by a violent blow on the leg. He survived this accident but three days,

and died after an intense fever, with delirium, to which succeeded great prostration, and coma. The veins in the neighbourhood of the wound offered nothing worthy of remark; but the crural vein was filled with coagulated blood, without, however, its parietes presenting any notable alteration. Examined by the microscope, this blood showed very small globules, and yet, among them could be discerned, here and there, globules of pus as perfect as could have been found in an abscess. In the other portions of the vascular system, the blood offered no peculiarities, either to the naked eye, or to the microscope. The inguinal glands upon the injured side were swelled and suppurating.

I will cite still another case, that of a woman who died at La Charité in consequence of a vast psoas abscess. Independently of this, I discovered the following lesions: numerous purulent collections, like those called metastatic, were in both lungs: the coats of the right crural vein were uncommonly thick, carnified, as it were, and their internal surface rugose and uneven. The blood filling this vein resembled sanies, and the microscope revealed in it a large quantity of pus-globules. But, in addition, these globules existed in the blood of the heart; a great number of them was found in the fluid blood of the right ventricle, and they were again met with, but in much smaller number, in the blood of the left ventricle, which was also fluid. A very small fibrinous concretion was entangled in the columnæ carneæ of this ventricle; in those of the right ventricle a membraniform web was interwoven, such as is found in the heart after all varieties of diseases, and deaths, and which is nothing more than a deposit of fibrine spread out like a membrane, as it is sometimes upon the surface of concretions. If I speak of it here, it is for the purpose of showing what degree of coagulability this pus-infected blood retained, and because I examined this sort of false membrane with the microscope, and found it constituted, like all fibrinous productions, by a very beautiful net-work, in whose meshes were imprisoned globules of blood and of pus, as perfectly distinct from one another, there, as elsewhere. In this case, too, where

blood and pus were mixed together at such different points of the circulatory system, I did not find the globules of blood differing either in number or general aspect, in form or size, from what they usually are in dead bodies.

These three cases prove clearly that pus, in the form of globules, can circulate with the blood in the vessels, and even pass through the lungs from the right to the left side of the heart. It seems to me very evident that it was so in the last case: the greater part of the globules, urged from the venous system into the pulmonary artery, stopped in the ultimate ramifications of this artery; whence the numerous abscesses that existed in the lungs; but some of them were able to enter the pulmonary veins, and reach the left side of the heart where I detected them.

In these various cases, the globules of pus appeared to me to remain as distinct from those of the blood, as they are when artificially mixed together in a vessel. I have often tried this experiment, and can give my assurance, that unless too little pus be mingled with the blood, the pus, on examination with the microscope, will be found to exist in it, under the form of well preserved globules: these even seem, in most cases, to unite together under the influence of a sort of attraction, so as to form little groups apart from the blood-globules, which do not appear to be in the least altered by the admixture. I have also determined by experiment, that on mingling directly pus with blood, the latter suffers no change appreciable by the naked eye, or by the microscope, nor any in the amount of its fibrine, so long as the pus is fresh. But such is not the case when pus, long separated from the body and partially decomposed, is mingled with blood; then the blood undergoes remarkable modifications, both in its appearance, and in its intimate structure, as the following experiment shows.

I left to itself, from June 6th 1842, to the 12th of the same month, some grumous pus furnished by a cold abscess. It remained for six days, in the sun, exposed to a high temperature. At the end of this time it diffused a putrid odour, and had blackened the diachylum which covered the vessel containing it.

I then had bled a patient suffering from acute articular rheumatism, and divided the blood into three equal portions. I mixed with the first its tenth part of the pus which had been kept for six days, and the whole was beaten together to extract the fibrine.

The second portion was left to itself, for twenty-four hours, without admixture of pus. At the end of this time it presented a well formed coagulum covered with a thick buffy coat, and surrounded by colourless serum. From the first and second portions I extracted the same quantity of fibrine, viz. $\frac{7}{1000}$. The solid part was even a little greater in the first, on account of the pus which had been added to it.

Finally the third portion of blood was, like the first, mixed with its tenth part of the same pus, and then left alone. An hour after this admixture I found a well formed coagulum, but without buffy coat, and surrounded with transparent serum. The pus, putrid as it was, seemed, then, to have had no peculiar action on the blood, (unless indeed it prevented the formation of a buffy coat,) it had not diminished its consistence.

But at the expiration of twenty-four hours, the condition of things had changed: the vessel was filled with a reddish liquid matter, like that obtained by adding ammonia to blood. There was no solid substance in this blood, except some fragments at the bottom of the vessel, and which together were hardly equal to a twentieth of the original clot. When subjected to the microscope, this liquid mass showed no traces of blood-globules; but a large number of pus-globules was found in it, so that putrefaction had not destroyed these latter. In the fragments forming the *débris* of the clot, pus-globules were also discovered, together with some remnants of blood-globules irregular in form, and of diminutive size. In these remains of the clot, the fundamental character of the fibrine was not lost, for the microscope revealed in it a net-work of fibres.

It is now proper that I should add, that having in other experiments, mingled with blood a tenth part of recent pus, taken from abscesses one or two hours before, and distinctly alkaline, in twenty-four hours I found the blood entirely coagulated,

and in no apparent manner differing from another portion of the same blood simply left to itself during twenty-four hours. These two portions of blood furnished me the same quantity of fibrine.

It is a clear deduction from these experiments, that the influence of pus upon the blood is far from being the same when the pus is fresh, as when it has been long enough withdrawn from the living body, to have become putrid. Fresh pus has no appreciable action upon the blood; putrefied pus acts like ammonia upon the blood, destroying at the same time both globules and fibrine. But it is remarkable that this destruction does not take place immediately. The contact must have lasted several hours before the blood begins to present any traces of alteration.

These results should incline us to believe, that in cases of disease where pus happens to circulate in the blood, the changes which the latter may experience in its constitution will vary according to the qualities of the pus which may chance to mix with it: if recent, the pus will leave the blood unharmed; if already old, and altered itself, it may become so potent a cause of disturbance to the blood, as to extinguish life suddenly and inevitably. But it is very remarkable that even in the second case, it is not the globules of pus which appear to affect the blood injuriously; I am much more disposed to believe that what then destroys both the globules of the blood and the fibrine, is something which is no longer pus, but the ammoniacal product formed at the expense of the pus itself.* And if, as can hardly be doubted, this ammoniacal product is that which remains upon a bistoury that has been thrust into a putrid subject, if it forms the basis of those deleterious emanations which escape from animal bodies, either dead, or in dense crowds while alive, we may understand how, in these cases apparently so dissimilar, the blood must undergo alterations, identical in their nature, and variable only in degree; and understand, also, how symptoms of the

* The excellent thesis lately presented to the Faculty of Medicine by M. D'Arcet may be profitably consulted in regard to this subject.

same order should result from causes which appear so different. And thus it is that inflammation, the essence of which is to make the blood more consistent, by increasing its fibrine, may bring about, remotely, the liquefaction of the blood by the destruction of its fibrine. This is what happens, if the pus created by the inflammation becomes mingled with the blood, after undergoing a preliminary alteration and decomposition within, or without, the place where it was formed. But the disease has then changed its nature, and the inflammatory state is replaced, or at least, overpowered, by the typhoid state; that is to say, instead of there being more, there is really less fibrine in the blood, than natural. The study of the alterations of the blood comes, then, to confirm one of the most important principles of pathology, namely, that in proportion as a disease passes through its several phases, it is modified, not only in its symptoms, but in its essence. Clinical and therapeutic facts, no less than those furnished by an analysis of the blood, do not permit our acceptance of the dogma maintained by Tommasini, that a disease, commenced with one diathesis, cannot change it during its course; that if sthenic in the beginning, it will remain so to the end, and that consequently its treatment should continue to be uniform from beginning to end.

I am unwilling to leave this subject, without saying a few words touching the influence of the ordinary antiphlogistic treatment upon the blood.

Amongst the various forms of this treatment depletion holds the first rank. I have then naturally to inquire, how far bleeding, repeated more or less frequently, has the power of removing the excess of fibrine in the blood, rapidly or gradually. Now it is found that however repeated or abundant the bleedings, the fibrine increases none the less, if these bleedings are performed in the early stages of an inflammation of some intensity, or, in other words, at the period of the ordinary increase of the disease; on the other hand the inflammation does not prevent there being found, after each bleeding, a progressive diminution of the globules. It seems, then, that when

once the blood has set about producing an excess of fibrine, no matter what is done, a certain time must elapse before this disposition is exhausted. Besides, this resistance of the fibrine to the action of depletions, and the development it acquires in spite of them, are perfectly in keeping with what takes place in the inflamed solid itself, and in the rest of the organism. The most copious loss of blood does not effect the immediate removal of the lesions of the solid; a certain space of time is always necessary for accomplishing this, and for the extinction of the fever. So that the fibrine, the quantity of which in the blood represents the degree of inflammation, obeys the same law which makes the latter continue for a certain time, and pass through certain stages. Let it not, however, be thought that I deny the utility of blood-letting, when properly employed, in this class of diseases. Experience has taught me, that without removing them suddenly, it often abridges their duration, and conspires to bring about a favourable issue. I even admit that if blood be drawn at the very outset of the inflammation, while yet there is nothing more than congestion in the solid, and the fibrine of the blood hardly above its normal standard, depletion may stop the progress of the disease, and, in certain cases at least, render it really abortive. But if the disease be a little farther advanced, this will not be the case: it is not in the power of art to prevent a well formed pneumonia from lasting seven or eight days at least, although it may prevent its being prolonged for a fortnight. You cannot arrest a well marked case of acute articular rheumatism within eight, twelve, and oftener, fifteen or twenty days; but by the use of blood-letting will more frequently see it arrested within the last named period, than if depletion had not been used. I will add a few words upon the modus operandi of the agents called revulsives.

I do not deny that this term often expresses a real action, by virtue of which the movement they attract towards the skin, or the digestive mucous membrane, may put an end to that which disease has developed at another point: I even believe that one or more fluxionary movements may be established

towards these membranes, which will diminish the activity with which the fluids tend to the part originally irritated and congested. But another influence of these revulsive agents, and one that has been less noticed, is that which they may have upon the composition of the blood, which they must modify by means of the materials which they extract from it. Thus a large blister takes from the blood a certain quantity of its serum; but, in addition, fibrine is deposited upon the raw surface produced by the action of the cantharides. If the blood should contain a superabundance of fibrine, would that be a means of diminishing its excess? Or, on the contrary, if the blister were large enough, if the resulting inflammation were very intense, if, above all, it increased the already existing fever, would there not result a new cause for the formation of an excess of fibrine in the blood, and would not this cutaneous inflammation, thus artificially created to diminish the intensity of another inflammation, and by the sort of influence it would have on the blood, augment the morbid condition which represents the inflammatory state in the blood, and is the measure of its intensity? As to purgatives, which are also employed as revulsives, it may be asked what is the nature of their influence on the blood, according to whether they chiefly excite the flow of perspiration, of mucus, or of bile, and what changes of composition they may occasion in the blood. This is undoubtedly an interesting subject for investigation.

ARTICLE V.

Of the Blood in Hemorrhages.

I DO not intend, in this article, to treat of the influence which profuse losses of blood may have upon the composition of that fluid; I have already spoken of this subject, and have stated that every hemorrhage certainly lessens the quantity of the globules, while, on the other hand, it must be very pro-

longed or very copious, to diminish in any appreciable degree the amount of fibrine. I propose, at present, to inquire how far all hemorrhages are due, originally, to some modification of the composition of the blood.

From the examinations I have made of this subject, I believe I may conclude that there is a certain number of hemorrhages whose cause cannot be traced to any primitive lesion of the solids, and which are the results of a change in the composition of the blood, consisting in a relative or absolute diminution of its fibrine.

And let us remember, at the outset, that the ancients ranked dissolution of the blood amongst the causes of hemorrhage. But what else is this dissolution, than a state of the blood in which it contains less fibrine than usual?

Let us also remember that hemorrhages are common in diseases where the blood contains but little fibrine, such as typhus fever and scurvy; that, on the other hand, they are rare in diseases where there is an excess of fibrine, either positively, as in the phlegmasiæ,* or relatively as in chlorosis.

In the diminution of the fibrine relatively to the globules, we must recognize the grand condition of the blood favourable to the production of hemorrhages; the relation of these two facts is so constant, that it seems to me impossible not to regard the one as the cause of the other. Let it not be said that the hemorrhage induces the diminution of the fibrine in the blood; for, as I have already stated, the loss of blood must be very copious to produce that effect, and I have seen the fibrine diminish where the amount of the hemorrhage could certainly not explain that occurrence. Finally, I may add, as an argument that appears to me unanswerable, that if the hemorrhage produced a change of the blood, in the cases under consideration, the globules should, unquestionably, be found diminished

* It may be objected that the sputa of pneumonia are almost always tinged with blood; but I reply that that is not an ordinary hemorrhage. The blood, which, in this disease, is mixed with the expectorated matter, is literally the result of its forcible expression through the parietes of the ultimate bronchial ramifications.

in a larger proportion, even, than the fibrine; but this is not the case, and so far from it, that the globules are most frequently in excess relatively to the fibrine.

Two very different conditions of the blood, in which the law of the diminution of the fibrine relatively to the globules persists, may predispose to hemorrhage.

The first of these is that in which the amount of globules has reached the highest limit of the physiological state, or has exceeded it, the fibrine meanwhile preserving its normal proportion, and standing at least as often below, as above, its average. This is what takes place in plethora, and common observation teaches us that plethoric persons are disposed to hemorrhage. Who is not familiar with their frequent epistaxes, and with the relief afforded by them? This is because these hemorrhages infallibly diminish the amount of globules of the blood, without affecting its fibrine; the equilibrium between these two elements is thus spontaneously re-established in these persons, and hemorrhages with symptoms of plethora are not renewed until an excess of globules is once more reproduced along with the blood.

But a second condition of the blood which is much more favourable than the preceding to the production of repeated and profuse hemorrhages, is that in which the quantity of fibrine is really under the standard, while that of the globules is natural. I have observed this in scurvy.

This disease resembles chlorosis, in some respects, and both have symptoms in common. In both may be remarked the same feebleness, the same dizziness, the same aberrations of sensibility, the same dyspnœa, the same palpitations, the same dyspepsia. But that which distinguishes scurvy from chlorosis is the readiness with which hemorrhage occurs in the former affection, so as to constitute one of its characteristic symptoms. And why do hemorrhages so constantly take place in scurvy, so rarely in chlorosis? Because in the former there is an alteration of the blood quite different from that in the latter. In scurvy the globules are not diminished as in chlorosis; on the contrary the fibrine decreases as we have

seen it do in typhoid fever of an adynamic or putrid type; a disease, which not less from its symptoms, than from the alterations it caused in the blood, had been very correctly styled *acute scurvy*, by Bordeu.

Well marked scorbutic cases are so rare in Paris, that for a long time I had to rest contented with mere conjecture concerning the state of the blood in scurvy, and had admitted, as very probable, that it must contain less fibrine than natural. I have at length been able, by observing the following case, to satisfy myself that my supposition was correct.

In the course of April, 1841, a labourer, forty-one years of age, entered my wards at the hospital of La Charité. For three years he had been wearing himself out by the daily toil of turning a crank in a dark and wet place, leaning against a wall from which the moisture was incessantly dripping. About once in every three weeks he indulged in wine to intoxication. He slept with seven comrades in a small, badly-lighted, and worse ventilated, chamber.

At the commencement of March, 1841, he suffered from vertigo, and a continual weariness that he could not account for; he felt sore and broken down, and soon was attacked with bleeding at the nose, which recurred every morning. A little later, red spots (as he called them) began to appear all over his body; these spots became more numerous, and larger, and, at the same time, his feebleness made such progress, that he was obliged to quit his work.

When this patient came under my notice, his trunk, limbs, and face, were covered with numerous petechiæ, and large ecchymoses, which might have been mistaken for bruises; but so far from there being such, on the succeeding days we saw others like them forming before our eyes. The gums were soft, swollen, and bleeding; the epistaxes continued, but sparingly. The patient complained of a general numbness, a heaviness of the head, and vertigo; he begged to be bled to put an end to these symptoms. The powers of digestion were still unchanged; there were some palpitations of the heart; *but no bruit de souffle in the carotids.* The pulse was 60,

the respiration 20, the temperature of the skin in the axilla 37.60. The great predominance of cerebral symptoms, and the idea that they might be caused by a sort of congestion, induced me to have the patient bled, and indeed he strongly desired it. I found in the blood, globules 119; solid constituents of the serum 86; and fibrine only 1.6.

After five weeks of rest, and substantial food, and under all good hygienic influences, this man regained his strength, and the symptoms of which I have spoken had, at least, much improved; yet a considerable number of petechiæ remained upon his skin, and his gums were still inclined to bleed. In this condition he went out on the 18th May.

The 23d May, he was again attacked with violent vertigo; his appetite was lost; he had a profuse epistaxis, and he returned to the hospital on the 2d of June. He was then extremely feeble; extensive ecchymoses covered his skin, and the conjunctivæ were so infiltrated with blood, that they protruded beyond the cornea, and surrounded it like a pad: the case might have been taken for one of double chemosis. Blood exuded from the gums and mingled with the expectorated mucus. I again examined the blood; it contained the same quantity of fibrine as at first; the globules had fallen to 111; the solid constituents of the serum remained at 86, of which 70 were albumen, and 9 of other organic matters. After some time the patient became much better, and went out.*

* Nothing is more difficult than the complete and ultimate cure of those diseases in which the blood is gradually and spontaneously despoiled, either of its globules or its fibrine. It is well known how easily chlorotic girls relapse, and how long it is before their symptoms disappear entirely. In older persons, who become anæmic spontaneously, the reproduction of the blood-globules is obtained with greater difficulty. As regards scurvy, that variety which arises under the influence of external causes, generally yields with as much ease, as soon as those causes cease to operate, as the other variety which arises spontaneously, often resists every means that may be brought against it. I have, it is true, seen some scorbutic patients recover, but I have seen a greater number whose disease, although at intervals appearing to improve, never totally ceased, and sooner or later became so aggravated as to induce a fatal termination.

Here then is a disease, in some sort, of the same type with all those in which more or less frequent and spontaneous hemorrhages arise in the same manner, and a remarkable alteration of the blood accompanies it, to wit, a diminution of fibrine. I have found the same kind of alteration of the blood in a case of scarlatina which terminated fatally on the second day of the eruption. In this case there were petechiæ all over the skin, a bloody exsudation within the mouth, and, at the autopsy, I found in the respiratory apparatus the anatomical signs of an extensive pulmonary apoplexy. The blood contained, fibrine 2, globules 133, solid constituents of the serum 81, of which 66 were albumen, and 6, other organic substances. I do not doubt that the fibrine of the blood would be found below its normal standard in all distinct cases of purpura hæmorrhagica: I can at least declare, that in a case of purpura whose symptoms resembled those of the severest typhus, I found the blood in that state of fluidity and dissolution which is the expression of its loss of fibrine.

But it is not only in these cases of repeated hemorrhage, or, if the term be preferred, of hemorrhagic diathesis, that I have seen the blood thus impoverished in fibrine. I have elsewhere cited cases of cerebral hemorrhage, where also the attack had been preceded by a diminution of the fibrine in the blood;* Hence, whether the blood escape from several tissues at the same time, or whether it find exit through a single one of them, facts lead us to admit, in the second case as in the first, that some hemorrhages take place because the blood, deprived of its natural proportion of fibrine, has, on that account, lost a portion of its plasticity. And thus we are led to find, in an alteration of the blood, the starting point of certain morbid phenomena, the cause of which is usually referred to a lesion of the solids. The cases in which the fibrine is only diminished relatively to the globules in excess, belong, by virtue of their symptoms, to the class of hemorrhages called active, and the cases in which the fibrine is really diminished belong to

* First Memoir upon the alterations of the blood, &c.

that of hemorrhages called passive. A somewhat minute investigation of the alterations of the blood lends a new support to this ancient classification, which though inadmissible into certain theories, is not the less essential, both in therapeutics, and in clinical instruction. In spite of every effort, it will never be possible to attribute identity of cause and nature, to the hemorrhage of a plethoric, and that of a scorbutic individual.

I have abundantly demonstrated, that the most usual impoverishment of the blood, that which results from the mere diminution of the globules, is not a direct cause of hemorrhage: yet it happens, from time to time, that hemorrhage is observed to come on, and to recur with disastrous obstinacy, in persons who have suffered from excessive loss of blood; but this fluid is then so far exhausted, that after having lost a great part of its globules, it has also parted with much of its fibrine. When this latter condition exists, hemorrhages may take place; so that their occurrence is connected with the last degree of impoverishment of the blood, not because the globules are then greatly diminished, but because the fibrine has, in its turn, given way. Besides, when blood enough is taken from an animal to destroy it, and this blood is divided into several portions for separate analysis, the fibrine is found less abundantly in the portions last drawn, than in the first. Profuse hemorrhages may, then, exhaust the blood of its fibrine, and this explains how it may happen, that towards the end of a very considerable hemorrhage, the blood may escape from other outlets than those from which it at first issued. I remember, for instance, having seen a young man whose whole cutaneous surface was covered with petechiæ, during the continuance of a copious epistaxis which could not be arrested; although, until that time, he had never had such symptoms. These facts being known, we can conceive how a hemorrhage, which has exhausted the system by its copiousness, and by its frequent returns, may find a cause of persistence and relapse in the new condition of the blood which it has created. Hence, one of the dangers resulting from large depletion resorted to

for the arrestation or prevention of hemorrhages; it may, from its excess, have the effect of perpetuating them or of bringing them back.

Hemorrhagic blood, as regards its physical properties, does not differ from that of the pyrexiæ. It never presents any buffy coat, without inflammatory complication. The clot is generally large, and never small, except in those cases of extreme poverty of the blood of which I spoke last. It is more commonly remarkable for considerable softness, and when the hemorrhage depends on a very great diminution of fibrine, the blood may be so little coagulable as hardly to form a veritable clot; or it may happen that, instead of this latter, there is nothing in the vessel containing the blood, except some disconnected lumps suspended in reddish serum. This is that state of dissolution of the blood of which I have already spoken under the head of the pyrexiæ, and which exists, more or less, in all the diseases characterized by a general disposition to hemorrhage.

I have already had occasion, in several places in this work, to insist upon the relation which may be shown between the dissolved state of the blood, and certain morbid phenomena; this is one of the most important facts in medicine, a fact very carefully studied by the observers of preceding ages, and from which the exclusive solidist doctrines of our day had entirely diverted the attention.* I have shown that this state of dissolution of the blood uniformly coincided with a diminution of the quantity of fibrine. But is this the ultimate alteration we are permitted to arrive at? Before the fibrine decreases, has there not been some other change of composition in the blood,

* Let me here be allowed to remind my readers, that in a work published in 1823 (*Clinique Médicale, t. I.*) I had admitted and described this state of dissolution of the blood in certain cases of low fever, and that I had pointed it out as capable of playing a part in the production of several of the symptoms of these diseases, and especially of the hemorrhages which so often accompany them. The investigations of M. Magendie have, more recently, thrown light on this important question of etiology. (See his *Leçons sur les phénomènes physiques de la vie,* 1837.)

of which the depression of the fibrine below its normal average is itself only the consequence? Upon this subject some facts may be cited. It may be remembered that on throwing into the veins of living animals, as M. Magendie has also recently done,* a concentrated solution of subcarbonate of soda, an almost fluid blood was found in the bodies of these animals when dead, and that, during life, their symptoms were analogous to those observed in diseases, in which the older writers admitted a state of dissolution of the blood. It may also be remembered that some authors declare, that they have found an excess of alkaline matters in the imperfectly coagulated blood of persons who died of low fevers or scurvy. I may also state that in the investigations which I am now pursuing in regard to the variations in the proportions of the inorganic constituents of the blood, I have found, amongst other things, that the blood most highly charged with free alkali belonged to the scorbutic patient whose history I have, a little while ago, related. This is a result analogous to that announced by M. Frémy, several years ago.

The different virulent and miasmatic substances which, on being introduced into the blood, diminish its coagulability, may, then, act upon the fibrine like the alkaline substances just alluded to. Thus, too, the venom of the viper may act, which, according to Fontana, produces a dissolution of the blood.

It has been said that extreme agitation of the nervous system may deprive the blood of its power to coagulate. According to several observers, a similar effect may be produced by a strong moral emotion, a concussion of the brain, the destruction of a certain portion of the spinal marrow, or a violent blow upon the pit of the stomach affecting the nervous plexuses of that region. If facts of this class were appropriately verified, they would, doubtless, be of the highest importance: for they would show that the nervous system exerts a powerful influence on the constitution of the blood, and that, conse-

* Magendie, t. II, p. 316.

quently, a lesion of innervation may deteriorate the blood, just as an alteration of the blood may modify the nervous action. For the very reason that such facts may have extensive bearings, we are unwilling to receive them at present, and we wait until new facts have stamped them with their proper value. Professor Dupuy of Alfort announced that by dividing the pneumogastric nerves in horses, the blood of these animals lost its property of coagulating. But, as it seems to be the fate of our science that it shall appropriate no truth that has not been, as it were, purified, by the test of contrary facts, the value of these experiments has been lessened by others of Dr. Mayer, in which, this *savant*, having tied the pneumogastric nerves in living animals, found that, uniformly, the blood had coagulated throughout the whole pulmonary circulation. These facts require a new examination. Nor shall we receive, without additional proof, certain other allegations, already old, from which it would result that the blood is found in a state of dissolution in animals killed immediately after being violently driven.

Whatever may be the truth regarding the number and the nature of the causes which render the blood less coagulable, it is not the less certain that there are some diseases in which the blood shows a strong tendency to dissolution, while there are others in which the blood becomes more coagulable. A learned Italian physician,* Bufalini, even regarded these two states of the blood of such importance, as to make use of them for dividing all diseases into two great classes: to one of these he assigns as cause what he terms the *phlogistic process*, and to the other an opposite state of the system which he designates by the term *process of dissolution* (processo dissolutivo). This division is equivalent to that which I have admitted, into diseases with an excess of fibrine in the blood, and those with less than the normal quantity of this principle; for in the latter there is evidently a cause whose effect is, necessarily, to make the blood less coagulable.

* Bufalini, *Fondamenti di patologia analitica*, Pesaro 1830, vol. ii, p. 327.

I cannot here refrain from a short discussion of a historical question, long ago proposed by Grant.* This author, who practised medicine, and wrote towards the close of the last century, suggested the inquiry whether the peculiar hygienic condition of the people of Europe before the eighteenth century, must not have caused them to be frequently attacked with diseases, one of whose principal elements, if not their starting point, was a state of dissolution of the blood. It is certainly very remarkable that the observers of preceding ages, constantly speak of dissolved and incoagulable blood, in their histories of epidemics. I readily admit that the theories then prevalent may have contributed to make this state of the blood appear more common than it really was. I know very well that there is more than one cause of error to be avoided in this case; that, during life, blood may seem less disposed to coagulate, merely because it has not run well from the vein, or been received in a proper vessel. I also know that blood which has coagulated, as usual, soon after the extinction of life, will subsequently become fluid, and that more or less speedily according to the temperature, after some degree of putrefaction has commenced in the body; I admit that these circumstances, and several others, may have been overlooked more than once, and that blood has been regarded as dissolved by disease, when it was so only from some accidental cause. Nevertheless, all the circumstances just enumerated were as well known by the ancients, as by ourselves; and if they have sometimes taken no account of them, it appears to me difficult to suppose that they should always have overlooked them. Besides, in some histories of epidemics, they are very careful to say that the blood had not the same aspect in the different stages of the disease, and that, for example, it formed a distinct clot at the commencement, while, at a later period, it hardly coagulated at all. This record of the changes experienced by the blood, in proportion to the progress of the malady, gives a great value to these descriptions. At an epoch nearer to our own times,

* Grant, *Recherches sur les fièvres*, Lefébure's translation, vol. I, p. 276.

Sarcone,* in his history of the epidemic of Naples, has spoken of the difference between the blood drawn at the commencement, and that drawn towards the termination of the disease.

"The blood," says this author, "was tenacious and buffy during the first week, and the first days of the second; at the end of the second week, its aspect changed, and it appeared to be more distinctly altered; the clot could be easily divided; a slight pressure was sufficient to break it up. . . .; lastly, these alterations still increased in the course of the third week, and especially that tendency to dissolution which appeared at the close of the second week. The blood, drawn from a vein, was converted into a thin, black coagulum, swimming in a dirty and bloody serosity."†

The disease in which Sarcone observed this alteration of the blood, is one of the last remnants of those great epidemics, which continually prevailed in Europe during the middle ages, and whose incessant re-appearance seemed attributable to the bad ventilation and food peculiar to those times. In those epidemics, which, indeed, often become endemics, nothing was more common than to observe gangrene, hemorrhage from various parts, extensive ecchymoses, or thousands of petechiæ covering the skin, while the general symptoms of our typhoid fever developed themselves with a high degree of intensity, and the greatest rapidity.‡ These pyrexiæ, with their assemblage of dangerous symptoms, and especially their hemorrha-

* Sarcone, Systematic account of the diseases observed at Naples during the year 1764, translated [into French] by Bellay, vol. 1.

† Huxham (treatise on fevers) has, in his narrative of the epidemic fever of Plymouth, described a much more complete dissolution of the blood than that mentioned by Sarcone. The blood of the patients, seen by Huxham, did not even present a distinct coagulum; the vessel appeared to contain nothing but a brown liquid, at the bottom of which was deposited a sort of reddish powder, formed by the separate particles of what should have been the clot.

‡ This is not the place to enter into detail as to the nature of the hygienic influences, which even at a period not very far distant, gave birth to and maintained in Europe those general diseases in which the alteration of the blood seems to play so important a part. Even men unfamiliar with the

gic form, rarely appear in these times, and, when observed, only as sporadic cases. Scurvy, as an endemic disease, has also disappeared, and now a few cases of it only are seen. This disease, the cases of which were formerly so numerous in Paris, can hardly be said to exist there at present, except by the traces it has left. But these different affections are, as it were, the external manifestation of the internal condition of the blood; we must therefore admit, that in consequence of the change in the nature of the influences which necessarily act upon men, the blood, which receives before the solids, the impression of the greater part of these influences, must present changes in its constitution proportioned to those undergone by the agents which operate upon it. It would appear, then, that there must have been a time when a very peculiar constitution of the blood engendered maladies, which, in certain respects, may have differed from those now observed, and may not have required the same treatment. And thus it is, that at different periods of the existence of our race, and through the diversity of influences to which it may be subjected, diseases of very different types may arise, and undergo changes in their essential nature which are revealed to us by the specific character of their symptoms. This too, is one amongst many reasons, why, according to the times, some theories may be received with peculiar favour, and explains

practice of medicine were, themselves, struck by it. Erasmus, the philosopher, who flourished towards the close of the sixteenth century, wrote that, in his day, the inhabitants of London were every year, from spring to harvest, attacked by a malignant fever, which committed the greatest ravages in that city, and especially amongst the poorer classes. I have been struck with the following details given by Erasmus of the causes to which he attributes this fever. "The supply of water," he says, "fails the inhabitants; they have to seek it at a great distance from the city; the river water is carried upon their backs, and is so dear that the poor cannot procure enough of it to wash themselves, and keep their houses clean. These houses are of wood, and very cold in winter, which makes it necessary to fill the rooms with straw. But as this cannot be often renewed, it becomes spoiled, and very injurious." I find this passage in Grant, who quotes it, (vol. i, p. 288, op. cit.)

how the development of these theories may be favoured by the very nature of the facts observed.

The dissolution of the blood has been regarded, at other epochs of our science, as connected with another state, which was held to be very common during the empire of the old humoral doctrines, I mean *putridity;* and as, in our day, this term has been revived by some persons, it is well to ascertain its meaning.

As long as the blood circulates in the living vessels, it is inadmissible to suppose that it can undergo a real putrefaction. Yet there is a certain number of diseases in which, after death, every part of the body, but especially the blood, much more speedily presents the signs of putrefaction, than in others, and these diseases are precisely those in which the blood has lost its coagulability during life. Independently of this common character, they have all a peculiar aspect; their ordinary phenomena being rapid prostration, fœtor of the excretions, and a tendency to hemorrhage, and gangrene. These the ancients considered as signs of the putrid state; but they are nothing more than signs of the diseases in which the spontaneously coagulable matter of the blood is more or less diminished. The rapidity with which putrefaction after death is observed to take place, in these cases, simply depends, perhaps, on the tissues being more promptly impregnated with blood, on account of its fluidity, which allows it to transude through the coats of the vessels very soon after the cessation of life. Let us also remark that, in the language of Boerhaave and Huxham, the phrases *dissolved state* and *putrid state* were synonymous. So that, in their numerous treatises upon diseases which they called *putrid,* the older writers have done no more than transmit to us their observations and their hypotheses touching that extensive class of maladies, in which the blood does not contain its normal quantity of fibrine,* and

* Schwenck thus describes the qualities of the blood in putrid diseases: "In morbis putridis, dissolutio cruoris advertitur, et a venâ emissus sanguis non coagulatur." (Schwenck, *Hæmatologia,* p. 129.)

these, moreover, they set in opposition to inflammatory diseases, just as our modern investigations authorize us still to do.

Long before Schwenck, Fernel had also noticed the absence of coagulation in the blood as one of the fundamental characters of putrid diseases. Upon this subject he expresses himself thus:

"Sanguis, qui per febres putridas detrahitur, sæpe animadvertitur putridus, adeo ut nec sibi cohærere, nec concrescere queat, omnibus scilicet ejus fibris putredine consumptis." (Fernel, *De febribus*, cap. v.)

In a very remarkable work of Huxham, entitled "*An essay on fevers, and on the different kinds of fevers which depend on the constitution of the blood,*" there is a chapter whose title is, "*On the dissolved and putrid state of the blood;*" and there Huxham has recorded a very interesting case, which appears to me eminently fitted to show the identity of nature of those diseases formerly called *putrid*, and those in which the blood has been proved, by analysis, to be spontaneously deprived of a certain quantity of its fibrine.

The subject of this case was a surgeon, who in October 1741 was seized, without known cause, with alternate rigors and flushes of heat, a weak pulse, loss of strength and appetite; and heavy respiration; he continued at his business in spite of the fatigue he experienced. Four or five days after his seizure, Huxham met him at a patient's house, and observed that his breath was fœtid. Two days after, he being at another patient's house, suddenly fainted. When he came to himself several livid and violet-coloured spots were observed on his hands and neck. On the way home, he fainted several times. The disorder increased every moment; he had extreme languor, and great oppression, with continual sighing; his breath was now insupportably fœtid, blood leaked from his gums, and a great many livid, violet, and black spots appeared all over his body, on the trunk, as well as the limbs.

Huxham continues the narrative as follows:

"He was bled to about ℥xii from his arm, but this gave him no manner of relief, the oppression, sighing, fainting, and anxiety continuing as bad as ever, nay rather increasing;—a violent hemorrhage also broke forth from his nose; which continuing from both nostrils, he was bled again to ℥x about twelve hours after the former bleeding:—neither did this give him any relief, but increased his weakness considerably, and he continued as anxious, restless, and oppressed as ever, without even the least sleep. The blood now not only issued from his gums and nose, but ..... in a surprising manner likewise dropped, though slowly, from the caruncle of one of his eyes; and several livid pustules on his tongue, and within side his lips, broke, and discharged a bloody, thin matter very copiously.

"The hemorrhage being somewhat restrained, a bloody dysentery came on with severe gripes, and excessive faintness, and he was still exceeding restless and very feverish: his pulse now intermitted every sixth or eighth pul-

ARTICLE VI.

Of the Blood in Dropsies.

It is at present, generally acknowledged that, while some forms of dropsy depend upon certain alterations of the solids, there are others again whose point of departure must be sought for in an alteration of the blood. It has been asserted also in rather a vague way that serous effusions might be the consequence of an impoverishment of the blood, or of what has been called hydroæmia. This opinion, I am now about to examine.

And in the first place, we may understand by the expression, impoverishment of the blood, very different conditions of that fluid. The blood may really have lost somewhat of its accustomed richness, from its containing either less fibrine, fewer globules, or less albumen than usual. In these three

sation, and then fluttered on again vastly quick; he had likewise a constant *tremor* and *subsultus*. The hemorrhage all this while continued from one part or other, and when stopped at one place forthwith burst out at another; so that his urine now seemed tinged with blood.... Soon after he was bled the second time, I was sent for, and hastened to him. I found him in the manner described, under an inexpressible anxiety, yet quite free from a delirium, though he had no manner of sleep for several days and nights: his tongue was vastly black, and his breath and stools insufferably stinking.

"I found that neither of the portions of the blood that had been drawn (not even the first) had separated into crassamentum and serum as usual, though the former had stood so many hours; but continued as it were half coagulated, and of a bluish livid colour on the top:—it was most easily divided by the slightest touch, and seemed a *purulent sanies* rather than blood, with a kind of *sooty powder* at bottom. His hemorrhage still continued, especially from the tongue, lips, and gums, with a perpetual dripping of bloody ichor from the nose; with never ceasing tremblings, *subsultus tendinum*, and almost continual faintings."—[An Essay on fevers, &c., by John Huxham, M.D., 3d edition, London, 1757.]

Huxham put this patient on the use of small and repeated doses of Peruvian bark, and various aromatic and astringent substances; he endeavoured to nourish him moderately, and succeeded in gradually restoring him to health.

cases, it should be equally regarded as impoverished; do they all then give rise to dropsy?

Diminution of the fibrine, to whatever extent it may have gone, does not certainly produce, as one of its consequences, the formation of this disease. In those morbid conditions in which the blood has lost no other principles than its spontaneously coagulable matter, we do not see effusions into the areolæ of the cellular tissue, any more than into the serous membranes, occur as an ordinary phenomenon. If these effusions are produced in that condition, it is the exception; and it becomes necessary, consequently, to seek some other cause for them than the diminution of the cipher of the fibrine.

Is the diminution of the globules, which, however slight, brings with it as a necessary result, the hydroæmic condition, a cause of the production of dropsy any more than the preceding? It is generally thought to be, and yet it seems to me that a somewhat rigorous observation does not permit us to adopt this opinion.

Were it true that dropsy was the ordinary consequence of a diminution of the globules of the blood, it ought to follow from this that the greater number of chlorotic patients, especially those who have the disease in a marked manner, should sooner or later become dropsical. But, this certainly is not the case. I have never seen the serous cavities filled with fluid in cases of simple chlorosis, nor have I ever observed a true anasarca; at most we may find in some chlorotic patients slight œdema around the malleoli, or slight puffiness of the eyelids, and that is all!

Neither have I observed dropsy to occur in men attacked with spontaneous anæmia, who, like chlorotic girls, had but a very feeble proportion of globules in their blood. I have said elsewhere that there is a kind of cachexia produced by the prolonged operation of saturnine emanations, a cachexia also characterized by a great diminution of the globules of the blood. I have treated many patients of this kind at La Charité, and have never observed dropsy in any of them.

Phthisical persons, in whom there generally exists a rather low cipher of globules, do not become dropsical, unless the pulmonary tubercles coincide with some other affection, whose effect is to give rise to serous effusions, as for example, disease of the heart, liver, or kidneys.

With the exception of chlorosis, I have rarely seen the globules descend to so low a cipher, and the anæmia become so marked as in individuals exhausted by some chronic organic disease of the stomach. In such cases there existed, in consequence of this considerable diminution of the globules, a well marked hydroæmia, and yet they presented me no trace of dropsy. In women labouring under cancer of the uterus, the blood comes insensibly to contain but very few globules, in consequence of the hemorrhages which many of these persons suffer from almost constantly; yet, we do not find dropsy supervening in these cases, any more than in the preceding; there was, for example, no trace of it in one of these women, whose case I have elsewhere cited, and whose blood contained only 21 in globules.*

Here then are many different cases in which, however impoverished the blood may have become in consequence of the

* I am not ignorant of the fact that, in some women who have cancer of the uterus, we find not unfrequently œdema of the lower extremities, or serous effusion into the abdomen; some have anasarca even. But, on the one hand, these various dropsies are not in such cases in proportion to the abundance or frequency of the uterine hemorrhages; and on the other hand, whenever I have met with them, I have been able to account for their presence by the existence of different alterations of the solids. Thus the œdema of the lower extremities was explained to me by tumours developed in the pelvic excavation, which compressed the crural veins, or by coagula formed in those veins during life. Cancerous masses, deposited in front of the vertebral column, a disease of the liver, a chronic peritonitis, tumours obstructing the circulation in the superior vena cava, or in the axillary veins, accounted to me for the occurrence whether of ascites, or of serous infiltration into one or both of the superior extremities. In the same way when cancer of the stomach is accompanied by ascites, we may affirm that the disease is not simple; and, if cancerous tumours do not exist in the peritoneum, we may be almost certain that the liver has participated in the degeneration of the stomach.

diminution of its globules, dropsy does not result. But, in all these cases, the blood has been slowly and gradually deprived of its globules. I have now to examine another condition, that in which the diminution of the globules has occurred rapidly and almost instantaneously: thus it happens in persons who lose suddenly a very large quantity of blood. Do we see dropsy establish itself more readily in such a case? I do not fear to affirm that, even in this case, serous effusions occur only as an exceptional condition; they are observed much less frequently than has been asserted after even very abundant bleedings; let us remark however that this cause produces them somewhat less rarely in children than in adults Neither do excessive spontaneous hemorrhages necessarily give rise to dropsies: I will cite as proof of this the case of a young woman who, a few days before her entrance into La Charité, and in good health up to that time, had had, in consequence of an abortion, a metrorrhagia so profuse that she resembled when I saw her, a chlorotic person in the most advanced stage; a very strong *bruit de souffle* could be heard in the heart and two carotids. This woman was so feeble and exhausted that it seemed as though she would expire in some of the continual syncopes which she fell into. During the following days, her strength improved somewhat; she retained however the paleness of death, and could not as yet make a movement without being threatened with fainting. It was necessary for two months to elapse before she could begin to leave her bed, and yet at the end of this time she still retained a *bruit de souffle* in the heart and carotids. During these two months, and afterwards, I sought with care for the slightest traces of dropsy in her case, but discerned none; the pressure of the finger produced not the slightest mark upon the malleoli. She had merely, as some chlorotic patients have, a slight swelling of the face, which is not œdema, for the skin in such conditions does not retain the impression of the finger.

I have seen so many cases like the preceding that I do not hesitate to assert that dropsy does not generally result, when the impoverishment of the blood depends simply upon the

diminution of its globules. Consequently, when it does occur, we should reasonably infer that the blood must, at the same time that it has lost some of its globules, have become impoverished in some other mode; and as it is not the diminution of its fibrine which can bring on this result, we may ask ourselves whether it be not owing to a diminution that shall have taken place in the albumen of the serum. Let us see what facts will reveal to us on this point.

There is a disease which, at the same time that it adds to the ordinary principles of the urine a certain amount of albumen, lessens more decidedly than any other the cipher of the albumen of the blood. Now, in this disease, which has the kidney for its seat, one constant phenomenon appears sooner or later; this is dropsy, which, at first partial and slight, ends by becoming general and very considerable. This dropsy augments in proportion as there escapes from the kidneys a larger quantity of albumen, and as we find less of it in the blood. Hence there are three facts which co-exist, disease of the renal parenchyma, diminution of albumen in the blood and dropsy. Is it the disease of the kidneys which produces the dropsy directly, as does an affection of the heart or liver? This cannot be admitted, for it is manifest that the kidneys exercise an influence upon the formation of the dropsy but indirectly, and in so much only as the change that has occurred in its texture allows it carry off from the blood its albumen. It is then the diminution of this latter, in the serum of the blood, which must be regarded as the true cause of the dropsy. Whatever then be the cause which makes this albumen diminish, dropsy will result. And moreover, it is not necessary, in order that this effect be produced, for the globules to diminish at the same time with the albumen. In Bright's disease, there is at first diminution of the cipher of the albumen alone, and the globules do not begin to decrease until later, when dropsy already exists.

Diminution of the albumen of the blood has, up to the pre sent period, been met with in man only in cases where this fluid has first lost a portion of its albumen through the kidneys

I have shown in another work,* that, in animals of the sheep kind, the diminution of albumen may occur, independently of the preliminary discharge of this principle by the urine; serous infiltrations also result from it occasionally in these animals, which helps to prove that their production is not in immediate dependence upon the disease of the renal parenchyma; but sheep in this case always have entozoa in the biliary duct. Is this then, a cause of the loss of albumen from the blood of those animals? We do not then as yet possess any well established case proving that the albumen, like the globules and fibrine, may spontaneously diminish in the blood, to an extent sufficient to produce disease. Nevertheless we have a right to affirm that there is but one kind of change of composition of the blood which results necessarily in the production of dropsy, and this alteration is the diminution of the albumen; consequently, whenever we see dropsy arise from what we suppose to be some modification experienced by the blood, we ought naturally to seek whether this fluid has not lost a portion of its albumen. Besides, it is not only from an excess of watery particles in the blood, that serous effusions are formed; for, if this were true, as I have before said, every chlorotic person should become dropsical, whereas, we see dropsy on the contrary, depending on another kind of alteration of composition of the blood, one in which it does not contain a great superabundance of water.

The dropsy which occurs towards the end of certain cases of scarlatina, seems to me equally to recognize as exciting cause a diminution of the albumen of the blood; for in this species of dropsy I have always found that the urine had become albuminous.

We sometimes see individuals who, having been exposed to some sudden cause of cold, are attacked a few hours after with anasarca. This accident, somewhat rare in our climates, is common on the contrary in equatorial regions. Upon what

* Mémoire sur la composition du sang chez quelques animaux domestiques.

depends this kind of dropsy? I long accounted for it by supposing that the sudden suppression of the cutaneous function of transpiration rapidly produced a superabundant exhalation of serum into the areolæ of the cellular tissue and the serous cavities. But a fact that I have recently observed permits me to explain otherwise the formation of this kind of dropsy. This fact is the following:

A young man, previously in good health and strongly constituted, enters the hospital of La Charité with considerable anasarca and commencing ascites. He relates to me that, a few days before, being abed and asleep, some of his comrades poured upon him a pot of cold urine, while he was in a state of perspiration. He got up naked in order to pursue them, and was very much chilled; he remained, said he, as though frozen. From the day following this occurrence, he began to perceive a slight degree of swelling, which rapidly augmented. I examined the urine of this patient, and found it albuminous. I concluded from this that the blood had been deprived by the kidneys of a certain amount of its albumen, and in this way accounted to myself for the formation of the dropsy. It is then upon the kidneys that the action of the cold had fallen. This dropsy was not, moreover, of long duration; at the end of a fortnight, the cure was complete.

Cases of dropsy following insufficient alimentation have been cited, and Dr. Gaspard has even reported a true epidemic of this kind, that prevailed in 1816, through several departments of the interior of France, as the result of a great scarcity which had afflicted those districts.* The inhabitants had been reduced to seek their food among the roots and herbs of the fields, which they cooked, etc. A large number of them became dropsical. History informs us that the same thing has occurred at other epochs under the influence of the same circumstances. It is probable that, in these singular epidemics, the insufficiency of alimentation must have modified the composition of the blood; that there was the point of departure of

* Journal de Physiologie expérimentale, par M. Magendie, tome ii.

the dropsy, and, after what I have said in the preceding pages, it is allowable to conjecture that the blood, under the empire of this influence, experiences a diminution of its albumen. What may still add some weight to this conjecture, is what takes place in sheep, when they have fed, for some time, in humid places, in pasturage of quality insufficient to furnish a good reparative material for their blood; in them also, the blood loses a portion of its albumen, and they become dropsical.

I shall not seek to discuss the question why blood, which has become poor in albumen, brings on readily the formation of serous effusions, and wherefore diminution of globules in the same blood does not produce a similar result. Is it the change effected in the physical qualities of the serum, by the loss of albumen which assists the passage of the former through the vascular parietes? Is this then a case of exosmosis favoured by the diminution in density of the fluid, or is it that the water of the blood flows with more difficulty in the capillary rete, because, being less charged with fibrine, it has become less unctuous, and slides perhaps less readily over the internal surface of the vessels? If it be so, the diminution of albumen in the serum of the blood would, as one of its effects, render more difficult the passage of this fluid through the small vessels, and consequently as to the immediate cause, there would not be so great a difference between dropsy following an organic disease of the heart or liver, and that which follows the diminished proportion of albumen in the blood.

Let no one believe however that, in cases of dropsy, there occurs only a separation of serum such as it existed in the blood; it is not so in any case of simple dropsy, for the constant rule is, that the serosity which has been effused, even while remaining composed of the same materials as the serum of the blood, contains proportionally more water than this, and much less of the organic principles, particularly albumen. Thus, in sixteen analyses that I have made of the fluids of different dropsies, I found for the maximum of albumen the cipher 48, and for minimum the cipher 4. In no case, there-

fore, was the quantity of albumen even equal to that which the serum of the blood contains. We may see moreover, by these extremes, how much the proportion of albumen contained in the fluid of dropsies may differ. In the sixteen analyses, I found the proportion of albumen in one thousand parts, represented by the ciphers, 48, 47, 41, 40, 30, 28, 19, 15, 14, 12, 12, 11, 10, 8, 6, 4. In six other analyses of serosity taken by puncture from the tunica vaginalis of the testis (cases of hydrocele), I found the albumen generally more abundant than in other effusions of serosity: thus, in these six cases, there was in albumen 59, 55, in two 51, 49, 35. The highest cipher in these six cases is far from equalling the mean of albumen in the serum of the blood. I have not observed in these different cases that the seat of the dropsy, any more than its cause, exercised an influence upon the greater or less elevation of the cipher of albumen; but it was different as to the more or less complete state of integrity of the constitution: in proportion as this remained stronger and more entire, so in general did the serosity effused contain more albumen. Here is very probably the reason why the fluid which came from the tunica vaginalis was usually richer in albumen than that of any other dropsy; because, in all these cases of hydrocele, the individuals operated upon were still full of health and vigour. In cases, on the contrary, where I have had occasion to examine the serosity taken from the abdomen of the same individuals by several successive tappings, I have constantly observed, that the more frequently the operation was repeated, the less abundant was the quantity of albumen contained in the serosity, which fact appeared to me to depend upon the progressively increasing debility of the constitution.

As to the water, I found it in all these specimens of serosity much more abundant than in the serum of the blood; its highest cipher was 986, and its lowest 930: consequently the effused serosity which had the minimum of water, still contained more than the serum of blood most highly charged with this principle: in this serum, in fact, we have found the maximum of the water for man 915; the minimum 725, and the mean

790. Besides it is in the serosity taken from cases of hydrocele that we have met with the least amount of water; it was in one of these cases that our minimum 930 existed, whilst the maximum of water for these same cases, was 947. On the contrary, in the sixteen other cases relative to serous effusions whether of the cellular tissue, of the pericardium, of the pleura, or of the peritoneum, this maximum 947 becomes almost the minimum; in all these cases, save two, we find more than 950 in water, 4 times from 950 to 960, and 10 times from 960 to 986.

Moreover, all these samples of serosity presented us, like the serum of the blood, fatty and extractive organic matters, an alkali, and alkaline and calcareous salts. The quantity of the saline matter appeared to us nearly similar to that of the same matter in the serum of the blood.

With the exception of our six analyses of the fluid of hydrocele, all the others are relative to cases where the dropsy was the result of some obstacle to the free return of the venous blood towards the heart; I much regret that none had any connection with Bright's disease. In these cases then, as in those of hydrocele, there is separated from the blood proportionally more of water than of albumen.

I have already said that the proportion of albumen separated from the blood, becomes more considerable when it is an inflammatory process which has provoked the effusion of serosity. This may be proved by an analysis of the fluid of vesicatories.

Cases, on the other hand, may present themselves where a fluid, similar to serum in its aspect, and like it alkaline, fails to show by re-agents any trace of albumen. This I have observed in the liquid, clear and limpid as rock-water, which is contained in hydatids of the liver. This fluid, slightly alkaline, was not sensibly clouded either by heat, by alcohol, or by nitric acid. It contained some alkaline chlorides, some sulphates, and much fatty matter.* Did the albumen which

* The fatty matter, which we find in serosity has at times a nature dif-

was absent from this fluid exist in the parietes of the living sac which contained it?

It is worthy of remark that, in a case where, in the same individual, there exists simultaneously several serous effusions in different parts, the fluids which constitute them may differ considerably from each other, as to the quantity of albumen which they contain. Thus, in a female attacked with an organic disease of the heart, there were 30 parts of albumen in the serosity of the pericardium, while there were but 4 in the serosity of the cellular tissue of the inferior extremities.

ARTICLE VII.

Of the Blood in certain diseases commonly called Organic.

I HAVE studied the composition of the blood in five cases of hypertrophy of the heart; in all of them the amount of globules was natural, as was, also, the albumen of the serum. Once only the fibrine showed a slight elevation, represented by 4. In the four other cases it preserved its physiological quantity, being represented by the numbers 2.6; 2.7; 3.0; and 3.7, respectively. These differences in the proportion of fibrine, bore a strict relation to those observed in the symptoms themselves. For, in the cases which gave 2.6, 2.7, and 3.0 of fibrine, the affection of the heart was chronic, and the pulse not accelerated. In the case which gave 4 of fibrine, the disease, on the contrary, presented a totally different aspect. The symptoms of the heart disease were only of two

ferent from that of the same matter ordinarily existing in the serum of the blood. It is thus that while examining with the microscope the fluid of a hydrocele obtained by tapping, I found in it crystals of cholesterine assuming the form of the purest parallelogram. To the naked eye the fluid psesented us, at the moment of its escape from the tunica vaginalis, a clouded appearance due to an infinity of little micaceous spangles which it held in suspension, and a great part of which were precipitated upon the bottom of the vessel by repose.

months' standing. They came on acutely during the course of an attack of articular rheumatism, and survived it. In addition to the signs of hypertrophy, a very distinct *bruit de souffle* might be heard at every contraction of the ventricles.

In the case where 3.7 of fibrine was found in the blood, that is to say, one of the highest maxima of the physiological state, the bleeding was performed under peculiar circumstances. There was no articular rheumatism, but a sudden exacerbation of the disease of the heart; the movements of this organ were excessively agitated, a very strong *bruit de frottement* was heard during both systole and diastole; the dyspnœa was extreme; the pulse beat 108 in a minute. The depletion was followed by great improvement, and, after a few days, the rubbing sounds had become much feebler. These facts teach us that the alteration of nutrition, which produces hypertrophy of the heart, does not affect the fibrine of the blood, when free from all complication; and that the increase of the fibrine takes place only under peculiar circumstances, and accompanied with symptoms which recall those of the inflammatory affections.

The mere deposit, within the tissues, of the morbid substances known as tuberculous, scirrhous, and encephaloid, and the development of hydatids, do not augment the fibrine. It may however, happen that at certain periods of the existence of these several productions, an excess of fibrine may be found in the blood, but that is because some other morbid condition has supervened. The following rules may be laid down in regard to this matter.

So long as tubercle and cancer preserve the character of hard masses, without any inflammation around them, an analysis of the blood uniformly gives the normal quantity of fibrine. But, as the softening of these hard masses advances, and a process of elimination, analogous to that of inflammation, is set up around them, the blood becomes more and more charged with fibrine; so that the excessive formation of this principle is not due to the development of the accidental production, but wholly to the inflammation excited by the latter

at certain stages of its existence. This is a new proof to be added to the many others which show that the process engendering the different accidental productions, such as tubercle, cancer, melanosis, hydatid, &c., is not of an inflammatory nature.

In order to justify the principles I have just laid down, I will first cite a very remarkable case, in which tubercles developed in the pia-mater simulated acute meningitis; but the qualities of the blood, even before the autopsy, excited doubts regarding the existence of the latter disease.

A sempstress, 24 years of age, entered the hospital of La Charité, May 27th 1841, complaining of having had a cough, and shortness of breath, for some time; she stated that she suffered from continual head-ache; on May 18th she met with a serious disappointment, and, a few days afterwards, her headache increased; from that epoch she experienced creeping chills. From May 23d she grew more seriously ill; on that day her headache was unusually severe, and, at the same time, she had humming noises in her ears, intolerance of light, and bilious vomiting. From the 27th to the 30th of May, the symptoms of an acute cerebral affection grew more and more distinct. From May 30th to the day of her death, which happened June 5th, she uttered piercing cries like those called hydrocephalic; there were delirium, strabismus, rigid flexure of the limbs; distressing moans and convulsive movements whenever the skin of the trunk or limbs, which seemed to have its sensibility greatly exalted, was at all rudely touched; and; towards the close, tetanic rigidity of the neck.

At the autopsy, the pia-mater was found thickly studded with tuberculous granulations, which were collected most numerously about the fissures of Sylvius. In no other part, either of the brain or its membranes, was any appreciable alteration detected. Tuberculous granulations similar to those which filled the pia-mater, were also found in the pleuræ of both sides, and in the peritoneum, both of which membranes were covered with them; both lungs were filled with miliary tubercles.

In this case, then, the only lesion revealed by dissection was the equal development in all the great serous membranes, and in the lungs, of small and hard tubercles, with no signs of inflammation around them. The anatomical characters of meningitis were completely wanting.

Let us look now at the analysis of the blood in this case. At the first bleeding we found 3.0 of fibrine, and at the second 3.4; so that the quantity of this principle did not exceed its physiological limits. While the patients lived, we were astonished at this result; it seemed strange that in a disease which appeared to us to be acute meningitis, the amount of fibrine should not be increased; the autopsy explained this anomaly, or rather showed us that the anomaly was only apparent. What evidence could be stronger than this, that whatever may be the extent or the rapidity of the formation of tubercles, it does not, in the beginning, augment the fibrine in the blood? An examination of the blood, in cases of pulmonary consumption, had already led me to lay down this proposition, in the first memoir I published with M. Gavarret. Since the publication of that memoir, we have collected additional, and confirmatory cases, of which the following is an abstract.

We weighed the fibrine obtained from the blood of thirty tuberculous patients, drawn at thirty-three different bleedings. In seven of these patients the tubercles were still crude; in nine others they were softening, and in the remaining fourteen, there were cavities in the lungs.

The six patients of the first series were bled, altogether, nine times. Seven times the fibrine was found to be normal, varying between 2.7 and 3.5. Twice, however, the fibrine exceeded its physiological quantity, and gave the numbers 4.8 and 5.1. But, in each of these two cases, there was an inflammatory complication; in one a sub-acute entero-colitis, and, in the other, a bronchitis of much greater intensity than is usual in the first stage of phthisis.

In ten bleedings performed on the nine patients of the second series, we already come to different results. Nine times out

of ten the fibrine was in excess, sometimes very slightly, hardly reaching 4, and sometimes varying between 4 and 5. In the tenth case, there were only 3 parts of fibrine.

In fourteen bleedings performed on the fourteen patients of the third series, the fibrine was in excess twelve times, but much more so than in the second series. The minimum found was 4.0, and that once only. In three other cases, the fibrine varied between 4.4 and 4.6; in all the others it was between 5.0 and 5.9.

The only two cases of the third series which did not follow the rule of the increase of fibrine, must be regarded as exceptional; the subjects of them were far gone in marasmus, when we attempted, by a small bleeding, to diminish the state of half asphyxia which they presented; and, indeed, they were momentarily relieved by it. In one of them the fibrine was at its physiological mean, in the other it had fallen to 2.0.

In the third stage of phthisis, therefore, although the fibrine is generally in excess, there are yet some cases, in which the exhaustion, consequent on the softening of the tubercles, is indicated by an opposite modification in the amount of fibrine; it augments during the process of elimination, and then diminishes, so as to fall even below the lowest limit of its physiological state.

Let us now examine how far the quantity of globules in the blood is affected by pulmonary consumption. This investigation will lead us to results worthy of some attention.

From the very commencement of pulmonary tubercalization, and when even auscultation can hardly detect its existence, the globules are already diminished. I have never seen them reach even their physiological average, 127, in any case of the kind. Their highest representative was 122, their lowest 99,* and they usually varied between 120 and 100, approaching the latter number oftener than the former. The blood of persons, then, whose lungs are beginning to be tuber-

* This minimum was found in the patient spoken of a little while ago, and whose serous membranes and lungs were thickly studded with tubercles.

culous, offers that particular modification which belongs to feeble constitutions; they are, truly, in a state of commencing anæmia, and their blood is like that of patients who have been bled several times. This condition of the blood which accompanies the first stage of phthisis, and which, to all appearance, precedes it, is the same general condition found in every case, where, from any cause, the powers of life have lost their energy. What need is there of saying that these results of analysis agree perfectly with clinical observation? Who is not familiar with that shrunken, pale, and feeble look, which belongs to most consumptives, even in the first stages of their malady? There are young girls, who, when consumption is imminent, become so frail and pallid, and yet have so few invocal symptoms, that it sometimes happens that the nature of their disease is misunderstood, and that they are supposed to be chlorotic. On the other hand, there are cases of chlorosis, which, owing to the complication of a bronchitis, or of a merely nervous cough, have thrown the most accomplished observers into doubt, and made them apprehend a development of tubercles.

In all commencing phthisis, there is, then, a certain degree of anæmia; but is that equivalent to saying that the impoverishment of the blood is the sole efficient cause of tubercles? Certainly not; for, in such case, a greater number of persons affected with phthisis would be found among chlorotic females than are so found, and I do not believe that girls with chlorosis become tuberculous oftener than others. The decrease of globules, from the outset of consumption, is not, then, a cause of the formation of tubercles, but we must regard it as a certain sign that this disease arises during a marked impairment of the constitution, and, by adding it to those signs furnished by the clinical observation of all ages, it helps to enlighten us in the choice and application of modes of treatment.

As the tubercles of the lungs advance, however, the diminution of the globules grows more and more considerable, and, at last, reaches its minimum when the lungs are filled with cavities. Yet, this minimum is not always what theory might

lead us to suppose it. It would seem, indeed, that in a disease in which the essential organ of hæmatosis is so seriously involved, and has become so unfit to fulfil its functions, the globules ought to diminish nearly as much as in chlorosis. But this is far from being the fact. In the second and third stages of phthisis, I have not yet seen more than a single case, in which the globules had fallen below 80; in it they were at 72, and the fibrine at 5.5. In all other instances they varied from 80 to 100. Is it not strange that in chlorosis, without any appreciable alteration of the lungs, or other solid, the globules should fall even lower than 30, while their minimum is at 72 in a disease in which it should seem that the state of the lung could hardly permit the formation of the blood, at all? And yet not only do the globules not diminish as much as might be expected, but, when even a large part of the lung is destroyed, the fibrine increases, and the temperature of the body may rise, just as in typhoid fever, or acute pneumonia. I have seen the temperature rise to 39° and 40° in the hectic fever which usually accompanies the last stage of phthisis.

I heard a *bruit de souffle* in the carotids of one only of the phthisical patients whose blood I analyzed, the same in whose blood the globules were at 72. This patient was a man about thirty years of age. The occurrence of the carotid *souffle* in him was well explained by the extreme poverty of his blood in globules; and its existence, in this single case, goes to corroborate the principles we have already laid down in regard to the connection of this sound with a certain decrease in the globules of the blood.

The appearance of the blood in the several stages of phthisis is well explained by the changes occurring in its composition.

In the earlier periods of the disease the blood offers no peculiarity, except that its clot is generally rather small and dense, which may be explained by the moderate quantity of its globules, and its preservation of a normal proportion of fibrine.

But with the progress of the disease, the softening of the tubercles, and the formation of cavities, the clot becoming

smaller and smaller, is covered with a buffy coat, the more perfectly formed in proportion to the degree of disorganization of the lung. Two circumstances evidently contribute to produce this buffy coat; the increase of fibrine which takes place so frequently in the last stage of phthisis, and at the same time, the progressive decrease of the globules; so that, there are two causes of an excess of fibrine relatively to the globules, and, if the blood flow in a proper manner, a buffy coat must necessarily be formed. This, indeed, is what happens, and a buffy coat upon the surface of the clot, is nearly as constant in the advanced stages of phthisis, as in pneumonia, or acute articular rheumatism. Considered in relation to the causes which govern its formation, it holds a middle place between the chlorotic, and the inflammatory, buffy coat.

Let us now examine the characters of the blood in cases of cancer. It may be inferred from the cases I have collected, upon this subject, that in cancer, as in tubercle, the fibrine of the blood does not increase until the scirrhous or encephaloid matter is advancing to, or has already reached, its stage of softening and destruction. Yet, if the cancer, owing to its situation, interfere with the functions of an organ, which is subservient to the reparation of the blood, this fluid may show a diminished quantity of fibrine. But that is a peculiar case.

In four cases of cancer of the stomach, we found the normal quantity of fibrine three times, in the fourth case it was less than this, being only 1.9.

In two cases of cancer of the liver, we found, on the other hand, a certain excess of fibrine in the blood; in one case 3.7, and in the other 5.0.

In the first case, the tumour of the right hypochondrium seemed to be in a state of transition between immaturity and softening: although usually indolent, it sometimes grew painful, and then a temporary fever was excited.

The symptoms of the other case were totally different; a patient had, in the region of the liver, a large, very painful and indistinctly fluctuating tumour, which had become rapidly developed, and was accompanied with continual fever. The

liver, in its whole extent, and beyond the place occupied by the tumour, was very much enlarged. The patient presented all the signs of an inflammatory affection so distinctly, that we conjectured the existence of a hepatic abscess. He sank rapidly, without our having, a few hours before his unlooked for death, seen any thing to indicate so sudden a termination. It was explained by our finding, on dissection, an immense effusion of blood in the peritoneal cavity. The source of this blood was a spongy cancerous projection, completely softened and ulcerated, and which occupied the free edge of the liver. Numerous encephaloid masses, reduced to a sort of *detritus*, filled the parenchyma of the liver, as well as several branches of the vena-porta.

In a case of cancer, ascertained by dissection to be ovarian, and which was accompanied with fever, and acute pains, the fibrine rose to 4.5. The cancerous mass was partially softened, and innumerable vessels traversed it in every direction. There were some traces of a slight peritonitis around it.

Finally, in two cases of cancer of the womb, we found that very different numbers expressed the quantities of fibrine; viz. 5.6 and 1.8. But the progress of the first case indicated a state of pretty intense phlogosis; the whole hypogastrium was tense and painful, and there was constant fever. In the second case there was complete apyrexia; the patient was thoroughly exhausted by repeated hemorrhage from the uterus. This was the remarkable instance of which I have already had occasion to speak, in which the blood contained only 21 parts of globules.

I have not, yet, had an opportunity of analyzing the blood of persons affected with hydatids, but, in sheep, I have often made this examination, and have always found the quantity of fibrine normal, where no other affection complicated the hydatids; but augmented, whenever an inflammatory process had been established around them.*

* Researches into the composition of the blood of certain domestic animals, &c.

In the several cases of cancerous disease I have just reviewed, the globules of the blood offered nothing remarkable, except the progressive diminution they undergo, whenever the organism is subjected to any cause whatever of exhaustion. The profuse hemorrhages which accompany some forms of cancer, the defective nutrition which must result from the greater number of cancers of the stomach, explain why, in many diseases of this nature, the blood is found sparingly supplied with globules. But this deficiency does not appear to take place in cancer, as in tubercles, at the commencement of the disease; it comes on late, and quite accidentally, from the causes just enumerated. The predisposition of the organism to form cancer, is not, then, like its tendency to form tubercles, expressed from the outset, by an impoverishment of the blood. It should be remarked, too, that, while from the very origin of his disease, and even before it is susceptible of demonstration, the tuberculous patient is always remarkable for his debility and paleness, such is not the case with one who has cancer. The latter may, before the commencement of his disease, and during its first stages, present every variety of constitution and temperament. What is more common than to see a cancerous affection in persons of a sanguine temperament, and who have the appearance of plethora? And what more rare, on the other hand, than the development of tubercles in such conditions of the system? Doubtless, there are not a few cases of young persons becoming tuberculous, amongst those who are fleshy, and have a ruddy complexion, with a certain appearance of strength: but the plethora of these individuals is deceitful, they have, in reality a lymphatic temperament, and if their blood be analyzed, its globules are found at, or even a little below, the lowest physiological limit.

There is ground for the question, whether, when once the cancerous cachexia is well established, there may not be an absorption of the cancerous detritus, and whether some traces of it may not be detected in the blood. To ascertain this, M. Gavarret and I have, several times, examined with a microscope, blood taken from the bodies of persons who had

died of various cancerous affections, and, in some instances, we found well formed globules of pus in the blood. These globules were not, indeed, portions of cancerous matter; they were merely a product of the inflammatory process, which, at a certain stage of the disease, is developed in the tissue where the cancer originates. Nevertheless, this is a fact in the history of cancer, important to be known, since it proves the possibility of a purulent infection of the blood, in this disease. In a case of osteo-sarcoma, with consecutive production of a large cancerous mass in the anterior mediastinum, we met with a large quantity of pus-globules mixed with the blood in the right ventricle of the heart. But along with these globules we found other bodies of an altogether peculiar aspect, and which we have, in this case only, detected in the blood. They were elliptical *lamellæ*, with a granite-like surface, much larger than globules of pus, and of a much more regular form than simple albuminous flakes. But these *lamellæ* were not found only in the right ventricle mixed with pus-globules. We found a great many of them in a little of the ichorous fluid taken from the centre of the cancerous tumour of the mediastinum. Are they, then, to be considered as denoting the presence of softened cancerous matter, or of the ichor which it furnishes? We can only say, that we have found the same *lamellæ* in other cancerous masses. The subject merits further investigation.

Before concluding this subject, I may add, that in a patient who died of ulcerated cancer of the liver, I detected the presence of some pus-globules in the thoracic duct; the contents of this vessel were reddish, and, along with the pus-globules, the microscope showed globules of blood, the most of them serrated at their circumference, and very distinct from globules of pus.

If, then, either before or during the development of these various accidental productions, one of the elements of their formation consists in some change effected in the composition of the blood, that change is, apparently, to be found neither in the fibrine, nor in the globules, nor in the albumen, but rather

in those numerous organic substances, mostly of an undetermined character, and which are comprehended in the term extractive matter. But are new substances generated? Are those which naturally exist modified in quantity or quality? What happens to the blood when tuberculous matter, instead of increasing, disappears, leaving a calcareous deposit in its stead? When accidental productions are formed of wholly inorganic substances, as by an accumulation of the salts of lime, what takes the place of these salts in the blood? What happens to the blood in those cases where the whole vascular system is filled with ossific concretions? Or what, when the bones are softened, and, being deprived of a large portion of their phosphate of lime, seem reduced almost to a cartilaginous state? Is it in some change in the composition of the blood, appreciable by analysis, that we are to look for the cause of those excessive secretions of uric acid that take place in gout and gravel? Medicine must wait for something of its advancement, till these, and many analogous questions, are resolved.

ARTICLE VIII.

Of the Blood in the Neuroses.

The title of this article may, at first, seem singular. For what could be found in the blood in diseases whose seat is the nervous system, whose symptoms are the various disturbances of the functions of that system, and which it is not customary to refer, either to an alteration of the solids, or of the fluids? I admit these notions, and yet I shall endeavour to prove, that even in the neuroses, the study of the state of the blood may be important.

Clinical observation has long since demonstrated, that one of the most powerful causes of many nervous disorders, is a certain degree of feebleness of the constitution; whence, the incontestable advantage of a tonic treatment, in many of these diseases, which by reviving the strength, restores the equili-

brium of the nervous system, and removes the disorder of its functions.

The results of an examination of the blood are confirmatory of those furnished by clinical experience.

Thus, it is found, that in many cases of neurosis, the globules of the blood are very scanty. Now it is well known that the increase or decrease of the globules of the blood, indicates the vigour or feebleness of the constitution. If the globules be diminished, either by depletion, or by insufficient nourishment, the nervous disorder will certainly be aggravated; but if the opposite course be pursued, in all probability the nervous affection will be mitigated. In this way may be explained the happy influence which the ferruginous preparations, and substantial and nutritious food, exert upon the termination of certain neuroses: and it is because the globules are inevitably diminished by depletion and diet, that we so often see such disturbance of the nervous functions follow great loss of blood, and a too prolonged abstinence from food.

But are we to be understood as declaring that such is the origin of every neurosis? Certainly not; there are diseases of this sort, and many of them, in which the quantity of globules in the blood is normal, and in which, even the aspect of the patient gives no indication of constitutional feebleness. In these cases, the blood has nothing to do with the production, nor with the maintenance, of the disease, whose etiology must be sought elsewhere, as well as the treatment most appropriate to it. These various facts are not inconsistent with one another; they only throw new light on one of the most important of medical truths, namely, that two diseases may have identical symptoms, without being of the same nature, and that however close their resemblance, they may, still, require different modes of treatment, because very different conditions of the economy may give rise to, or maintain, them.

THE END.

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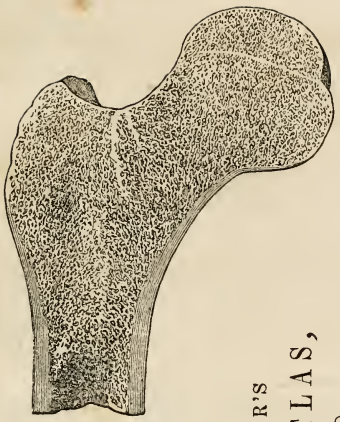

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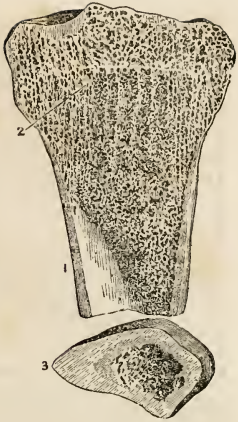

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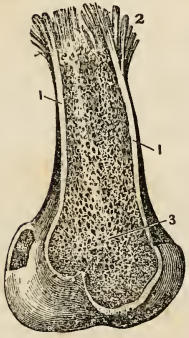

FIG. 7.

FIG. 4.

A Longitudinal section of a Femur, showing the Cellular Structure at its extremity.

FIG. 5.

A Longitudinal section of a Tibia, showing

1. The Compact Structure.
2. The Cellular Structure.
3. A Transverse section of the Femur, showing its Compact Substance, its Internal Cellular Structure, and the Medullary Canal.

FIG. 6.

The Texture of a Bone as shown in a Humerus, after maceration in dilute acid.

1. 1. The Compact Matter as usually seen.
2. 2. The same split, so as to show the Longitudinal Fibres composing it.
3. The Internal Cellular Matter.
4. The Bone seen under its Articular Cartilage.

FIG. 7.

A view of the Concentric Lamellæ of the Compact Matter of a Bone.

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